Visual Processing in Dementia and Mild Cognitive Impairment

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Submitted in partial fulfilment of the requirements for the degree of Doctorate in Clinical Psychology

Institute of Health and Wellbeing
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Kevin Murray

FOREWORD

The Major Research Project included in this clinical research portfolio was amended from an original version due to the impact of the COVID-19 pandemic. The original research proposal is included in Appendix 2.8, and the project aimed to generate new data by administering neuropsychological assessments via face-to-face contact with participants. As this method of data collection was not possible due to COVID-19 restrictions, the updated Major Research Project included in this research portfolio utilised existing data from electronic medical records.

CHAPTER 1: Systematic Review

Can Tests of Visual Impairment Aid Differential Diagnosis in Dementia?

A Systematic Review

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ABSTRACT

Background: As many as 32.5% of individuals experiencing neuropsychological decline display some form of visual impairment as part of their disease aetiology, and extensive research supports the inclusion of tests of visual perception in wider neuropsychological assessment to determine whether an individual is displaying symptoms of dementia. However, less is known about the extent to which these tests can help differentiate between different types of dementia. **Aims:** The current review examined the extent to which tests of visual perception can help to differentiate between different types of dementia. In addition, the review aimed to evaluate the methodological quality and risk of bias of included studies. **Methods:** Three research databases were searched for studies which satisfied the inclusion and exclusion criteria. Data from relevant studies were extracted and results synthesised. Included studies were reviewed for risk of bias and methodological quality using the QUADAS-2 and STARD guidelines. **Results:** Fourteen studies were included in the review. A low risk of bias was observed in relation to index test and reference standard, and there were few concerns regarding the applicability and clinical utility of results. A high risk of bias was identified regarding patient selection, and STARD ratings for methodological quality ranged from 25–38. Evidence was provided to support the finding that tests of visual perception can differentiate between Alzheimer's Disease and other types of dementia. In particular, those with Alzheimer's Disease typically outperform those who have Dementia with Lewy Bodies on these tests, but perform worse than those with Frontotemporal Dementia. **Conclusion:** There is evidence that tests of visual perception can aid differential diagnosis in dementia. However, improvements in the quality of research in this area is needed as well as greater understanding of the diagnostic accuracy of these tests.

Key Words: Dementia; Visual Perception; Differential; Diagnosis;

INTRODUCTION

Background

Visual impairment is a common problem for people with a diagnosis of dementia. This can include impairments in visual acuity, experienced by as many as 32.5% of dementia patients (Bowen et al, 2016), or with visual perception functions such as visuo-spatial processing, cited by Geldmecher (2003) as the most common form of visual impairment in dementia.

Several tests commonly used to assess neurocognitive ability include measures of visual processing, including the Addenbrookes Cognitive Examination (Hsieh et al, 2013), the Repeatable Battery for the Assessment of Neuropsychological Status (Randolph et al, 1998) and the Severe Impairment Battery (Saxton et al, 1990). However, there remains overlap between the different visual processes required for these tests, for example between visuo-spatial function, defined by Simic et al. (2013) as "*processes involved in perceiving spatial location, orientation, direction and distance*" (p1119), and visuo-constructional ability, defined as "*skills needed to put together parts to form a single whole*" (Simic et al. (2013; p 1119)).

The 'type' of neurocognitive decline can have distinct effects on visual perception. Although Alzheimer's Disease and Dementia with Lewy Bodies can both lead to impairments in visual processing, memory impairments are often the first noticeable symptoms in Alzheimer's Disease (Gottesman and Stern, 2019). During the early stages of disease onset however, individuals with Dementia with Lewy Bodies are reported to experience more severe visual impairments as part of their disease aetiology than those with Alzheimer's Disease (McKeith et al, 2017), and these visual impairments are more likely to include visual hallucinations and visual perception difficulties (Rosenblum et al, 2021). However, Dementia with Lewy Bodies is often misdiagnosed as Alzheimer's

Disease due to overlapping symptoms including problems with memory and language (Thomas et al, 2018).

Misdiagnosis of the specific dementia type an individual is experiencing can lead to the inappropriate treatment and management of symptoms, as well as inaccuracies relating to prognosis. Thorough assessment and accurate diagnosis of dementia type is, therefore, essential for providing appropriate post-diagnostic support, and visual assessment has been proposed as one method for improving clinical judgement in this area (Possin, K.L., 2011).

Aims

The current review aimed to examine the extent to which tests of visual perception can help to differentiate between different types of dementia. In addition, the review aimed to evaluate the methodological quality and risk of bias of included studies.

METHODS

The review adhered to the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) statement (Page et al., 2021), and the following sections outline the review protocol.

Search Strategy

The Ovid platform was used to search EMBASE, Medline and APA PsychINFO databases for relevant studies. The international database of prospectively registered systematic reviews (PROSPERO; University of York, 2019) was also checked to determine if there were any similar reviews in progress. The 'PICO' framework was utilised to help focus the search strategy, as outlined below:

Population: The inclusion criteria included studies involving adults (i.e., those aged 18 and over) with a confirmed diagnosis of dementia. Studies involving participants with unconfirmed or undiagnosed dementia were excluded.

Intervention: The studies included did not involve direct intervention. Rather, performance on tests of visual perception included within commonly used neuropsychological assessments were reviewed.

Comparison The inclusion criteria involved studies which aimed to identify scores on tests of visual perception and compare those obtained by individuals with different types of dementia (i.e., comparison of performance between at least two distinct dementia groups). Studies which aimed to utilise tests of visual perception to differentiate between individuals with dementia and individuals without dementia, or with individuals with other neurocognitive disorders (e.g., Huntington's Disease, Alcohol Related Brain Damage) in the absence of a diagnosis of dementia, were omitted by the exclusion criteria.

Outcome: The review aimed to evaluate the methodological quality of studies which used tests of visual perception to differentiate between different types of dementia. The outcome measure of interest for these studies therefore included visual perception ability, which was assessed using various different neuropsychological assessment tools, as outlined above. To satisfy the inclusion criteria, only studies which reported results of tests of visual perception were included. Qualitative studies, and studies not published in English, were excluded from the review.

EMBASE, Medline and APA PsycINFO were searched to identify articles which included the following terms in either Abstract, Keyword or Title:

(Dementia) AND (Differenti OR Distin*) AND (Visu*)*

These search terms were determined after scoping searches indicated that they were commonly used in studies comparing performance on tests of visual perception between different forms of dementia. No limit regarding publication date was set. After the search was conducted and the initial studies were identified, duplicates were removed and the remainder were screened for appropriateness using titles and abstracts. The remaining full text articles were then examined, and reference lists of included studies were also reviewed to identify any additional studies of relevance.

An independent rater replicated this search and, following the removal of duplicates, repeated the above process for 10% (n=211) of the total search results in order to determine inter-rater reliability. The independent rater identified all three studies included by the investigator in the sample, in addition to three studies which had been excluded by the investigator, resulting in 'substantial' (k=0.66) agreement. Agreement was reached to exclude the three additional studies as two did not measure visual perception, and one did not compare groups with a confirmed diagnosis of dementia.

Methodological Quality

Included studies were assessed for risk of bias using the Quality Assessment of Diagnostic Accuracy Studies 2 (QUADAS-2; Whiting et al, 2011). The QUADAS-2 includes 18 questions and was developed to assess risk of bias and concerns about applicability in studies related to diagnostic accuracy. Risk of bias and concerns about applicability are rated across three domains; patient selection, index test and reference standard. A fourth domain, flow and timing, is also rated for risk of bias. Domain-specific signalling questions are also provided for each domain, for example 'Was a consecutive or random sample of patients enrolled?'. Potential responses indicating low risk of bias include 'Yes' and 'Low', whereas 'No' and 'High' indicate a high risk of bias for that particular item. Concerns Regarding Applicability are rated as either 'Low' or 'High'. For

both risk of bias and concerns about applicability, items can be rated ‘Unclear’ if there is insufficient evidence for rating.

Unlike many risk of bias tools the QUADAS-2 emphasises that overall or mean numeric scores should not be generated to summarise a study. Instead, studies receiving a rating of ‘High’, ‘No’ or ‘Unclear’ on one or more items within a domain should be considered to be ‘at risk of bias’ or presenting ‘concerns regarding applicability’ within that domain. The signalling questions, including potential responses, for each domain are outlined in Appendix 1.2.

Included studies were also assessed for reporting quality using the ‘Standards for Reporting Diagnostic accuracy studies’ (STARD; Bossuyt et al, 2015). The STARD includes 31 items aimed at providing international consensus guidelines for assessing the reporting quality of studies investigating diagnostic accuracy. Prompt questions are provided which relate to six domains including, Title and Abstract, Introduction, Methods (including Study Design, Participants, Test Methods, Analysis), Results (including Participants and Test Results) and Discussion (Appendix 1.3). Each item is rated either 0 (information missing), 1 (some information present but insufficient detail) or 2 (information present) to provide an overall score out of 62.

An independent rater assessed 50% of the included studies using the QAUDAS-2 and STARD in order to determine whether assessment scores were reliable. This resulted in ‘substantial (k=.74) and ‘almost perfect’ (k =.81) agreement between the raters for QUADAS-2 and STARD ratings, respectively. Discrepancies in scoring were discussed in order that consensus could be reached.

RESULTS

Outcome of Search Process

The search process identified 3535 initial studies. As the PRISMA 2020 (Page et al., 2021) flow diagram in Figure 1 illustrates, this included 1425 duplicate studies. The titles and abstracts of the remaining 2110 studies were reviewed, and application of the selection criteria resulted in the exclusion of a further 2072 studies. The full text of 38 remaining studies were screened for eligibility, of which 13 were excluded as they did not include measurement of visual perception. Dementia diagnosis was not confirmed for 4 additional studies, and 8 studies did not include a comparison between different dementia types. References listed in each of the 13 remaining papers were examined, and 1 additional study satisfying the selection criteria was subsequently identified.

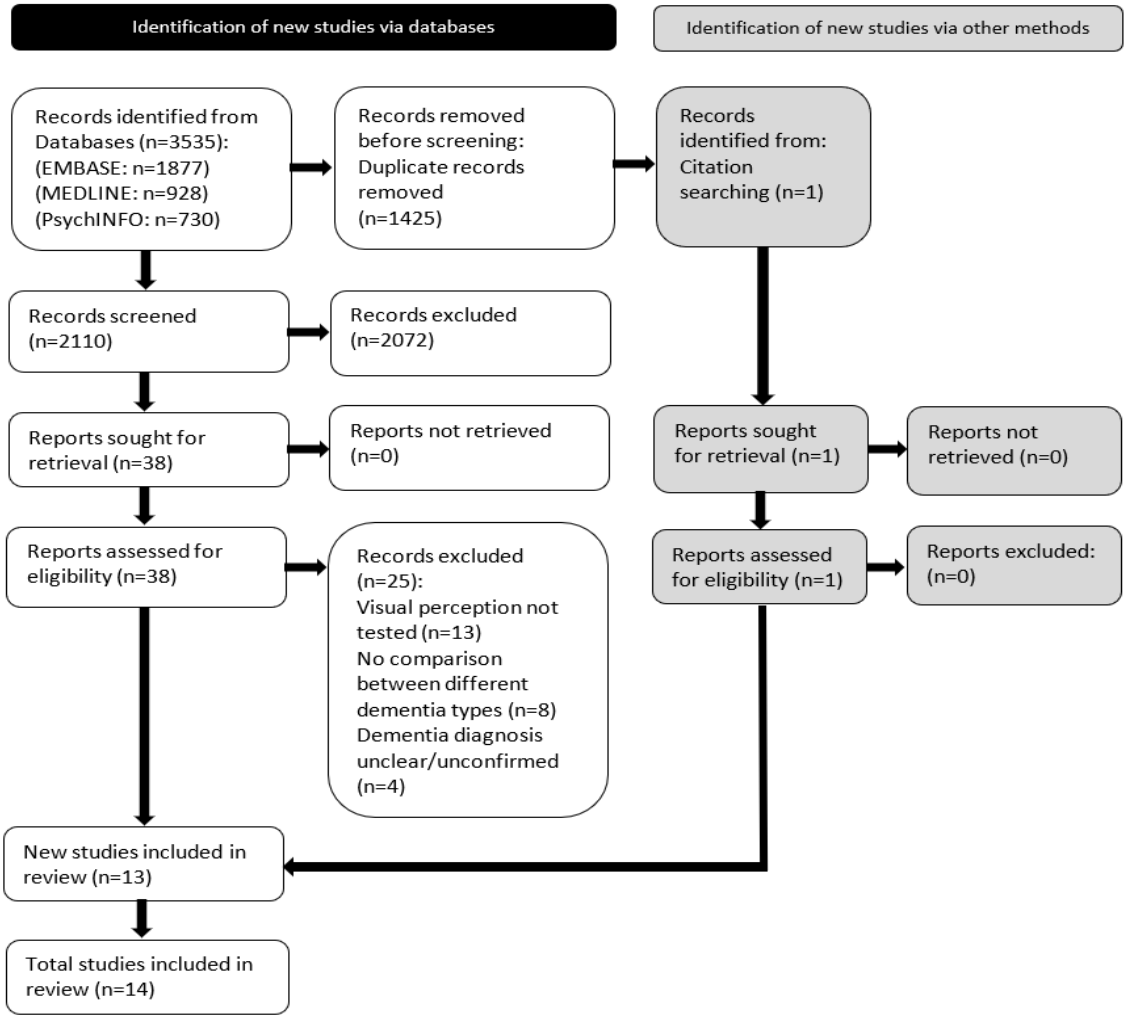

Figure 1: PRISMA 2020 flow diagram for systematic reviews

Study Characteristics

The fourteen studies included in the review were examined for participant information and test characteristics. Table 1 outlines data relating to dementia types and sample size, gender, age and education of participants included in each study along with the tests used and the results and outcome of each study.

Table 1: Characteristics of studies included in the systematic review

Study	Dementia Type (Sample Size)	Gender (M:F)	Age (SD)	Years Education (SD)	Test(s) used	Mean score (SD) / Other outcome	Results/ Findings
Prats-Sedano, M. A. et al. (2020)	DLB (76)	64:12	74.8 (6.3)	11.8 (3.1)	Addenbrooke's Cognitive Examination Revised (ACE-R: Mioshi et al, 2006): Visuo-spatial test	10.2 (3.9)	No sig diff. between DLB & AD on VS sub-test; Memory:VS ratio ≥1.1 differentiates DLB/AD (sensitivity=82%; specificity=68%)
	AD (40)	28:12	73.8 (8.6)	12.5 (2.9)		12.3 (3.4)	
	HC (66)	42:24	72.6 (6.9)	14.1 (3.4)		15.6 (0.8)	
Pouzeta, A. et al. (2019)	AD (32)	9:23	66.4 (5.9)	10.5 (3.3)	Visual Object and Space Perception Battery (VOSP: Warrington and James, 1991): Number Location	5.31 (3.03)	Significantly lower scores for AD group compared with SD group (p=.015)
	bvFTD (20)	15:5	72.7 (7.3)	10.6 (5.5)		6.63 (3.28)	
	SD (35)	18:17	71.3 (8.4)	9.6 (3.1)		7.67 (2.88)	
Salimi, S. et al. (2019)	AD (55)	31:24	65.0 (8.1)	12 (3.1)	a) ACE-R/ACE-III (Mioshi et al, 2006): Visuo-spatial test b) Rey-Osterrieth Complex Figure Test (RCF: Osterrieth, 1944)	a) 12.8 (0.4) b) 22.0 (1.3) c1) 9.1 (0.2) c2) 18.5 (0.3) c3) 6.5 (0.5)	Scores for AD group were significantly lower than those for bvFTD group on ACE-R/ACE-III ($F(1, 95)=5.2$, $p=0.025$) and RCF ($F(1, 93)=4.8$, $p=0.031$)
	bvFTD (51)	27:24	62.0 (7.5)	11.5 (2.7)		a) 14.1 (0.4) b) 26.3 (1.4) c1) 9.3 (0.2) c2) 18.9 (0.3)	

					c1) VOSP: Dot Counting c2) VOSP: Position Discrimination c3) VOSP: Cube Analysis	c3) 8.3 (0.5)	
	HC (54)	20:34	65.4 (7.7)	12.4 (2.6)		a) 15.55 (0.8) b) 32.6 (2.8) c1) 9.9 (0.5) c2) 19.8 (0.6) c3) 9.1 (1.7)	
Scharre, D.W. et al. (2016)	AD (21)	13:8	75.1 (5.0)	14.7 (2.1)	a) Mini Mental State Examination (MMSE: Folstein et al, 1975): Pentagon Copy b) Self-Administered Gerocognitive Examination (SAGE: Scharre et al, 2010): Visuo-spatial task (3D copy and Clock drawing task)	a) Correctly copied by 66.7% of group b) 2.19 (1.17)	DLB group performed significantly worse on MMSE Pentagon Copy task (p=.0126) and Visuo-spatial tasks of Self-Administered Gerocognitive Examination (p=.0161)
	DLB (21)	13:8	74.0 (4.8)	15.6 (2.6)		a) Correctly copied by 23.8 % of group b) 1.29 (1.31)	
	PD (21)	13:8	72.4 (4.7)	14.9 (2.3)		a) Correctly copied by 72.2% of group b) 2.86 (0.91)	
Park, L.Q. et al. (2015)	AD (240)	89:164 (overall sample; group level gender not specified)	78.7 (8.2)	14.1 (6.5)	The Measurement of Everyday Cognition Scale (ECog: Farias et al., 2008): Visuo-spatial sub-test	2.87 (0.96)	AD group significantly more impaired on task than FTD group (β=-0.34, SE=0.13, p=.01)
	FTD (13)		71.2 (11.4)	13.6 (3.2)		2.20 (0.96)	
Giovagnoli, A.R. et al. (2008)	AD (77)	[18:45]*	65.5 (9.9)	8.9 (4.9)	a) Raven's coloured progressive	a) 14.71 (7.50) b) 10.72 (9.11)	AD group significantly more impaired on RCF (F(2, 165)=154.79,

	FTD (40)	[35:15]*	61.1 (10.7)	8.9 (4.1)	matrices (Raven, 1936) b) RCF Copy (Osterrieth, 1944)	a) 16.08 (9.31) b) 17.31 (10.73)	p<.001); difference between groups on Raven's test not significant
	HC (91)	41:50	62.3 (10.0)	11.3 (4.4)		a) 31.27 (4.71) b) 32.87 (2.93)	
Kandiah, N. et al. (2009)	AD (78)	41:37	72.0 (8)	5.9 (SD not specified)	a) Wechsler Memory Scale Revised (WMS-R: Wechsler, 1987): Visual Reproduction test b) Clock Drawing Test (Shulman et al, 1986) c) WAIS-R (Wechsler, 1981) Block Design	a) 30.2 (SD not specified) b) 3.45 (SD not specified) c) 12.2 (SD not specified)	AD group performed significantly better than SIVD group on all tests of visuo-spatial ability (p=.005, p=.018, p=.001)* **Statistical values not reported*
	SIVD (78)	54:24	70.0 (9)	4.5 (SD not specified)		a) 23.4 (SD not specified) b) 2.73 (SD not specified) c) 6.80 (SD not specified)	
Charles, R.F & Hillis, A.H. (2005)	AD (15)	4:11	69.3 (11.7)	Not specified	a) Cortical Vision Screening test (CORVIST: James et al, 2001)** b) RCF Copy (Osterrieth, 1944)	a) 5.86% overall group errors b) 25.19 (8.1)	AD group performed significantly better than PCA group on CORVIST (p<.001) and RCF (p<.001)
	PCA (15)	4:11	65.3 (6.6)	Not specified		a) 34.3% overall group errors b) 7.34 (5.9)	
Tiraboschi, P. et al. (2006)	AD (94)	49:44	74.8 (8.4)	14.4 (3.3)	a) Dementia Rating Scale (DRS): Construction test b) MMSE: Pentagon Copy	a) 45% of group displayed Visuo-spatial impairment b) 16% of group displayed Visuo-spatial impairment	AD group performed significantly better than DLB group on Dementia Rating Scale – Construction subscale; Odds ratio (95% C.I.) = 3.5 (1.3-9.7); No

	DLB (23)	13:10	73.7 (4.8)	14.7 (2.8)		a) 74% of group displayed Visuo-spatial impairment b) 30% of group displayed Visuo-spatial impairment	significant difference in scores on MMSE (p=.1)
Graham, N.L. et al. (2003)	AD (19)	9:10	68.9 (8.6)	13.1 (3.4)	a) RCF Copy b1) VOSP: Letters b2) VOSP: Silhouette b3) VOSP: Object Decision b4) VOSP: Dot Counting b5) VOSP: Number Location b6) VOSP: Cube Analysis	a) 27.5 (11.0) b1) 17.7 (5.1) b2) 19.8 (5.7) b3) 17.6 (3.0) b4) 9.7 (0.6) b5) 8.1 (3.0) b6) 7.8 (2.7)	AD group performed significantly better than VD group on VOSP Silhouette task (Wald's $X^2(1)=4.58$, $p<.05$, odds ratio = 1.18); No significant difference in scores on remaining VOSP tasks or RCF Copy
	VD (19)	14:5	71.2 (7.8)	11.6 (3.1)		a) 22.0 (10.6) b1) 17.1 (2.8) b2) 15.6 (4.5) b3) 15.6 (3.3) b4) 8.8 (2.0) b5) 7.3 (2.2) b6) 6.8 (3.1)	
	HC (19)	9:10	68.1 (6.3)	11.3 (1.1)		a) 33.9 (1.6) b1) 19.2 (0.8) b2) 21.5 (2.7) b3) 17.2 (2.4) b4) 9.9 (0.3) b5) 8.7 (3.4) b6) 10.2 (2.6)	
Ala, T.A. et al. (2001)	AD (27)	13:14	79.7 (7.6)	12.1 (3.3)	MMSE: Pentagon Copy	Correctly copied by 59% of group	AD group performed significantly better than DLB group (Fisher's exact test, p=.002); failure on task associated with DLB with sensitivity of 88%
	DLB (17)	11:6	75.0 (7.2)	13.6 (3.3)		Correctly copied by 12% of group	

							(95% CI, 0.64-0.99), specificity of 59% (95% CI, 0.39-0.78)
Elfgren, C. et al. (1994)	AD (17)	6:11	66.0 (SD not specified)	Not specified	Block Design Test (Wechsler, 1958)	Median score = 0/24	AD group performed significantly worse on Block Design Test than FTD group (Stanine scale scores = 2, 3, *p*=.003)
	FTD (11)	4:7	58.0 (SD not specified)	Not specified		Median score = 13/24	
Yamamoto, E. et al. (2017)	AD (57)	26:31	71.8 (10.0)	Not specified	Montreal Cognitive Assessment (MoCA): Clock Drawing task	1.91 (0.81)	AD group performed significantly better than DLB group (p<.001; D=0.58)
	DLB (73)	42:31	73.3 (7.3)	Not specified		1.40 (0.88)	
Gnanalingham, K.K et al. (1997)	AD (25)	12:13	75.7 (1.4)	9.9 (0.4)	a1) Clock face test: Draw part a2) Clock face test: Copy part (Libon et al, 1993)	a1) 3.7 (0.5) a2) 5.5 (0.7)	AD group performed significantly better than DLB group on Draw part (p<.01)* and Copy part (p<.01)* of Clock face test **Statistical value not reported*
	DLB (16)	8:8	76.4 (1.8)	11.0 (1.1)		a1) 2.4 (0.4) a2) 2.4 (0.6)	
	PD (15)	10:5	72.6 (2.1)	10.3 (0.9)		a1) 6.2 (0.7) a2) 7.1 (0.8)	
	HC (22)	13:9	73.3 (1.3)	10.1 (0.5)		a1) 8.2 (0.2) a2) 9.6 (0.1)	

Abbreviations: AD (Alzheimer's Disease); bvFTD (Behavioural Variant Frontotemporal Dementia); DLB (Dementia with Lewy Bodies); FTD (Frontotemporal Dementia); HC (Healthy Controls); PCA (Posterior Cortical Atrophy); PD (Parkinson's Disease); SD (Semantic Dementia); SIVD (Subcortical Ischemic Vascular Dementia); VD (Vascular Dementia)
*M:F ratio as reported in study **Total CORVIST scores (individual sub-test scores not reported)

As Table 2 outlines, the fourteen studies included 1,577 participants across 34 different groups. This involved five different dementia groups, and five studies also included a 'healthy control' (i.e., non-dementia) group. All studies included an Alzheimer's Disease group, and the majority of overall participants (N=797, 51.2%) had this diagnosis.

Table 2: Aggregated patient characteristics by dementia type and overall

Dementia Type	N Groups (% of total)	N Participants (% of total)	M:F	Mean Age*	Mean Years Education*
Alzheimer's Disease	14 (41.2)	797 (51.2)	241:239**	73.3	12.0***
Dementia with Lewy Bodies	6 (17.6)	226 (14.5)	151:75	74.3	12.9**
Frontotemporal Dementia****	6 (17.6)	170 (10.9)	83:87	65.4	10.6***
Healthy Controls	5 (14.7)	252 (16.2)	147:105	67.6	11.6
Posterior Cortical Atrophy	1 (2.9)	15 (1.0)	4:11	65.3	(Not reported)
Vascular Dementia*****	2 (5.9)	97 (6.2)	68:29	70.2	5.9
Total	**34**	**1557**	**675:512****	**71.4**	**11.5*****

** Means reported are pooled means based on 'Dementia Type' groups*
*** Excludes data from studies which did not report gender ratio (Park, L.Q. et al. (2015); Giovagnoli, A.R. et al. (2008))*
**** Excludes data from studies which did not report Mean (Elfgren, C. et al. (1994); Charles, R.F & Hillis, A.H. (2005); Yamamoto, E. et al. (2017))*
*****Includes Behavioural Variant Frontotemporal Dementia group (Pouzeta et al., 2019; Salimi et al., 2019) and Semantic Dementia group (Pouzeta et al., 2019)*
******Includes Subcortical Ischemic Vascular Dementia group (Kandiah et al. 2009)*

Quality Assessment

Risk of Bias – QUADAS-2

The outcome of the QUADAS-2 risk of bias and concerns regarding applicability assessment for each study is detailed in Table 3, and individual ratings for each study are presented in Appendix 1.2.

Table 3: Outcome of QUADAS-2 risk of bias assessment

Study	Risk of Bias				Concerns Regarding Applicability		
	Patient Selection	Index Test	Reference Standard	Flow & Timing	Patient Selection	Index Test	Reference Standard
Prats-Sedano et al., 2020	H	L	L	Unclear	L	L	L
Pouzeta, A. et al., 2019	H	L	L	H	L	L	L
Salimi, S. et al., 2019	H	L	L	H	L	L	L
Scharre, D.W. et al., 2016	H	Unclear	H	Unclear	L	L	L
Park, L.Q. et al., 2015	H	L	L	H	L	L	L
Giovagnoli, A.R. et al, 2008	H	L	L	Unclear	L	Unclear	Unclear
Kandiah, N. et al., 2009	H	L	L	Unclear	L	L	L
Charles, R.F & Hillis, A.H., 2005	H	L	L	Unclear	L	L	L
Tiraboschi, P. et al., 2006	H	Unclear	H	Unclear	L	Unclear	L
Graham, N.L. et al., 2003	H	L	L	Unclear	L	L	L
Ala, T.A. et al., 2001	H	L	L	Unclear	H	L	Unclear
Elfgren, C. et al., 1994	H	Unclear	H	Unclear	L	Unclear	L
Yamamoto, E. et al., 2017	H	H	H	Unclear	L	Unclear	L
Gnanalingham, K.K. et al, 1997	H	L	L	Unclear	L	L	L

**Shaded boxes indicate High/Unclear risk of bias/Concerns regarding applicability*

As Table 3 highlights, all studies displayed a high risk of bias for patient selection. This was due to each study utilising a case control design, whereby participants were assigned to groups based on pre-determined dementia diagnoses. Considering the aims and hypotheses

of the studies involved however, it would have been difficult to apply a non-observational study design. However, studies involving recruitment based on consecutive referrals could have limited the risk of bias regarding patient selection.

The majority of studies displayed a low risk of bias in relation to index test and reference standard. For most (N=11) studies the results of the index test(s) were interpreted without knowledge of the relevant reference standards. Similarly, for most (N=13) studies there was a low risk of bias regarding the interpretation of the reference standard, and prior dementia diagnoses had been informed by thorough neuropsychological assessment across various cognitive domains. However, risk of bias relating to the flow of participants through the studies was difficult to assess due to limited or unclear information regarding how missing and indeterminate data were addressed.

As Figure 2 highlights however, overall there were minimal concerns regarding the applicability of results. Most studies sufficiently outlined the clinical implications of their findings, although some (Tiraboschi et al., 2006; Elfgren et al., 1994; Yamamoto et al., 2017) did not comprehensively relate these to the review question.

Risk of Bias		
Flow and Timing	High (3)	Unclear (11)
Patient Selection	High (14)	
Index Test	Low (11)	Unclear (3)
Reference Standard	Low (10)	High (4)
Concerns Regarding Applicability		
Patient Selection	Low (13)	H. (1)
Index Test	Low (10)	Unclear (4)
Reference Standard	Low (12)	Unclear (2)

Figure 2: Proportion of studies displaying Low, High and Unclear risk of bias and concerns regarding applicability
**Shaded boxes indicate High/Unclear risk of bias/concerns regarding applicability*

Reporting Quality Assessment: STARD

Individual STARD ratings for each study are presented in Appendix 1.4, and as Table 4 outlines overall STARD ratings ranged from 25 to 38. The mean overall STARD score was 33.4. Similar common issues to those identified within the QUADAS-2 were noted, including inadequate descriptions of missing and indeterminate data, and of the flow of participants through the study. Also, all studies failed to adequately justify sample size, and most offered insufficient detail on setting, location and dates relating to data collection.

Table 4: STARD quality assessment outcomes

Study	STARD Score	Study	STARD Score
Prats-Sedano et al. (2020)	35	Charles and Hillis (2005)	34
Pouzeta et al. (2019)	35	Tiraboschi et al. (2006)	34
Salimi et al. (2019)	38	Graham et al. (2003)	36
Scharre et al. (2016)	33	Ala et al. (2001)	28
Park et al. (2015)	37	Elfgren et al. (1994)	25
Giovagnoli et al. (2008)	33	Yamamoto et al. (2017)	30
Kandiah et al. (2009)	34	Gnanalingham et al. (1997)	36

However, most studies provided an appropriate and detailed summary of study design, methods, results and conclusions as well as a thorough scientific and clinical background to the relevant index test(s). The methods for estimating or comparing measures of diagnostic accuracy were described well overall, with cross tabulation of results and participant demographics generally well presented.

Synthesis of Results by Test(s) Used

The main findings for each study are presented in Table 5 (below). Of the eighteen different tests used, five were included in more than one study: ACE-R/ACE-III Visuo-spatial sub-test; MOCA Clock Drawing/Clock Face Test (Draw); MMSE Pentagon Copy; RCF; VOSP (Number

Location). Tests which have been used to compare at least two different dementia types, and where those disease comparisons have been replicated in more than one study, have been synthesised below.

Table 5: Tests and dementia types included in studies

Test	AD	DLB	FTD	HC	PCA	VD
ACE-R/ACE III: V-S	Prats-S.	Prats-S.		Prats-S.		
	Salimi		Salimi	Salimi		
Block Design Test	Elfgren		Elfgren			
Clock Test: Copy	Gnana.	Gnana.		Gnana.		
MOCA Clock Drawing/ Clock Test: Draw	Gnana.	Gnana.		Gnana.		
	Kandiah					Kandiah
	Yamamoto	Yamamoto				
CORVIST	Charles				Charles	
DRS: Construction	Tiraboschi	Tiraboschi				
ECOG: Visuo-Spatial	Park		Park			
MMSE: Pentagon	Scharre	Scharre				
	Ala	Ala				
	Tiraboschi	Tiraboschi				
Ravens Progressive M.	Giovagnoli		Giovagnoli	Giovagnoli		
RCF: Copy	Giovagnoli		Giovagnoli	Giovagnoli		
	Charles				Charles	
	Graham			Graham		Graham
SAGE: Visuo-Spatial	Scharre	Scharre				
VOSP: Cube Analysis	Graham			Graham		Graham
VOSP: Dot Counting	Graham			Graham		Graham
VOSP: Incomplete L.	Graham			Graham		Graham
VOSP: Number Location	Pouzeta		Pouzeta			
	Graham			Graham		Graham
VOSP: Object D.	Graham			Graham		Graham
VOSP: Silhouettes	Graham			Graham		Graham
WMS-R: Visual Rep.	Kandiah					Kandiah

Abbreviations: AD (Alzheimer's Disease); DLB (Dementia with Lewy Bodies); FTD (Frontotemporal Dementia); HC (Healthy Controls); PCA (Posterior Cortical Atrophy); VD (Vascular Dementia);
**Tests in shaded boxes used in more than one study*

ACE-R/ACE-III Visuo-spatial sub-test

The Visuo-spatial sub-test of the second and third versions of the Addenbrookes Cognitive Examination (ACE-R; ACE-III) were included in studies by Prats-Sedano et al. and Salimi et

al. As Salimi et al. identify, there is a high correlation between these tests, with the only difference relating to the drawing of interlocking infinity diagrams in the ACE-III as opposed to interlocking pentagons in the ACE-R. A study by So et al. (2018) found no significant difference in visuo-spatial scores between test versions (Z=-.895, p=.371; So, M. et al, 2018).

Prats-Sedano et al. found that individuals with Alzheimer's Disease (M=12.3, SD=3.4) performed significantly better than those who had Dementia with Lewy Bodies (M=10.2, SD=3.9; U=1041.5, p=.005). However, Salimi et al. found that those with Alzheimer's Dementia performed significantly worse (M=12.8, SD=.4) than those with Frontotemporal Dementia (M=14.1, SD=.4; F(1, 95)=5.2, p=.025). It was not possible to statistically combine the results of these studies however as they did not compare ACE-R/ACE-III Visuo-spatial scores between similar disease groups.

MOCA Clock Drawing /Clock Face Test (Draw)

The clock drawing tasks in Gnanalingham et al., Kandiah et al. and Yamamoto et al.'s studies involved drawing an analogue clock face and placing the hands at 'ten minutes after eleven o'clock'. Kandiah et al. found that individuals with Alzheimer's Disease obtained a mean score of 3.45 (SD not reported), whereas those with Subcortical Ischemic Vascular Dementia performed worse with a mean score of 2.73 (SD not reported). This difference was found to be significant (p=.018).

Gnanalingham et al. and Yamamoto et al. both found significant differences between the performances of individuals with Alzheimer's Disease and Dementia with Lewy Bodies. In Gnanalingham et al.'s study participants with Alzheimer's Disease performed better (M=3.7, SD=.5) than those with Dementia with Lewy Bodies (M=2.54, SD=.4; p<.01). Similarly, Yamamoto et al. reported a higher mean score for those with AD (M=1.91, SD=.81) than those with Dementia with Lewy Bodies (M=1.4, SD=.88; t(128)=.58, p<.001). Unfortunately, as Gnanalingham et al. did not report a statistical value or effect size, and Yamamoto et al. did

not report a precise *p* value, it was not possible to synthesise the results of these studies. As the results of the QUADAS-2 highlight however Yamamoto et al.'s study displayed a high risk of bias in relation to index test and reference standard, meaning that any synthesis of results between these studies would perhaps offer limited clinical or theoretical value.

MMSE Pentagon Copy

The Pentagon Copy task within the MMSE was included in studies by Scharre et al., Ala et al. and Tiraboschi et al. to compare between individuals with Alzheimer's Disease and those with Dementia with Lewy Bodies. In all studies, a higher percentage of individuals in the Alzheimer's Disease groups produced correct copies of the pentagon (66.7%, 59.3%, 84.0%) than in the Dementia with Lewy Bodies groups (23.8%, 11.8% and 70%). Scharre et al. and Ala et al. found these differences to be significant (p=.0126; p=.002), with Tiraboschi et al. obtaining results approaching significance (p=.10). Ala et al. and Tiraboschi et al. reported sensitivities of 88% (95% C.I., .64-.99) and 30%, and specificities of 59% (95% C.I., .39-.78) and 84%, respectively, regarding the use of failure on the pentagon to discriminate between Alzheimer's Disease and Dementia with Lewy Bodies.

Combining the results of the three studies indicate an overall mean of 76.7% and 37.9% correctly copied pentagons in the Alzheimer's Disease and Dementia with Lewy Bodies groups, respectively.

Synthesis of Results by Dementia Type

There were five different dementia types included across the fourteen studies, and all studies involved a comparison between Alzheimer's Disease and another disease type. As Table 6 outlines, there were 27 overall between-group comparisons between Alzheimer's Disease groups and other disease types. These comparisons included 19 different tests of visual perception. In all comparisons, Alzheimer's Disease groups performed better than Dementia with Lewy Bodies (N=9), Vascular Dementia (N=10) and Posterior Cortical Atrophy (N=2)

groups across 16 different tests of visual processing. All of these results were significant, with the exception of the MMSE Pentagon task within Tiraboschi et al.'s study.

Although the Alzheimer's Disease groups outperformed Dementia with Lewy Bodies groups in six different studies, and Vascular Dementia groups in two different studies, this effect was observed in a comparison against Posterior Cortical Atrophy in a single study only. This study, by Charles and Hillis, demonstrated a high risk of bias regarding patient selection, but low risk of bias relating to index test and reference standard, and low concerns regarding applicability in these areas. When compared with Frontotemporal Dementia however, Alzheimer's Disease groups performed worse in each of the six measures used, and only Pouzeta et al.'s study failed to find a significant effect for this difference.

Table 6: Performance of Alzheimer Disease groups compared with other dementia types on tests of visual perception

AD>Dementia with Lewy Bodies			**AD>Vascular Dementia**		
Study	**Test**	***p***	**Study**	**Test**	***p***
Prats-S. et al.	ACE-R/III Visuo-sp.	.005	Graham et al.	RCF: Copy	<.001
Scharre et al.	MMSE Pentagon	.0161	Graham et al.	VOSP Incomplete L.	N.S.
Scharre et al.	SAGE	.0126	Graham et al.	VOSP Silhouettes	<.001
Tiraboschi et al.	DRS-Construction	.011	Graham et al.	VOSP Object Disc.	N.S.
Tiraboschi et al..	MMSE Pentagon	.1	Graham et al.	VOSP Dot Counting	<.05
Ala et al.	MMSE Pentagon	.002	Graham et al.	VOSP Number Loc.	N.S.
Gnana. et al.	Clock Draw	<.001	Graham et al.	VOSP Cube Analysis	<.01
Yamomoto et al.	Clock Draw	<.01	Kandiah et al.	WMS-R V-R	.005
Yamamoto et al.	Clock Copy	<.01	Kandiah et al.	Clock Draw	.018
			Kandiah et al.	Block Design	.001
AD>Posterior Cortical Atrophy					
Study	**Test**	***p***	**Study**	**Test**	***p***
Charles and Hills	CORVIST	<.001	Charles and Hills	RCF: Copy	<.001
AD<Frontotemporal Dementia					
Study	**Test**	***p***	**Study**	**Test**	***p***
Giovagnoli et al.	Raven's P.M.	<.001	Pouzeta et al.	VOSP	.301
Giovagnoli et al.	RCF: Copy	<.001	Salimi et al.	ACE-III Visuo-sp.	.025
Elfgren et al.	Block Design	.003	Park et al.	E-Cog	.01

**Non-significant p values in shaded boxes*

DISCUSSION

The current review demonstrates that, at a group level, individuals with Alzheimer's Disease typically outperform those with Vascular Dementia, Dementia with Lewy Bodies and Posterior Cortical Atrophy, but perform worse than those with Frontotemporal Dementia, on tests of visual perception.

However, although the QUADAS-2 ratings indicated few concerns regarding the clinical applicability of results, little is known about the diagnostic accuracy of these tests or whether specific cut-off scores could be used to contribute to determining dementia type. It remains difficult, therefore, to suggest to clinicians how results from these tests might be interpreted to inform decisions regarding differential diagnosis. Whilst there may be group-level differences in performance on tests of visual perception, there may nevertheless be considerable overlap between groups in distribution of test scores. Therefore, at an individual level patients with two different aetiologies may both score within an average range on a test. Without cut-off scores to indicate what level of performance might be characteristic of different dementia types, it may not be possible to use individual test scores for differential diagnosis. It may be more productive, however, to combine neuropsychological test scores from a range of domains, perhaps in combination with other biomarkers such as magnetic resonance imaging (MRI) or cerebrospinal fluid (CSF) markers to determine if the patterns of scores are more accurate in predicting dementia type. One example of this approach is tested in Tolonen et al., (2018) in which a disease state index classifier model, utilising neuropsychological, MRI, and CSF data, is used to predict the likelihood of a patient falling into one of five categories: controls with subjective cognitive decline; dementia due to Alzheimer's disease; vascular dementia; frontotemporal lobar degeneration; dementia with Lewy bodies.

In addition, the overall quality of research in this area could be improved. In particular, many of these studies display a high risk of bias relating to patient selection and fail to adequately

illustrate or report the participant's journey ('flow') through the study. Many studies fail to provide sufficient detail regarding the time interval between the index test and reference standard, although these items were described and reported adequately in most cases. These issues could be addressed by recruiting participants based on consecutive referrals, thereby simplifying and standardising the 'flow' of participants through the study and perhaps helping to clarify the time interval between the reference standard and index test.

Limitations of the Review

Although the studies included all addressed the overall review question, the review was unable to improve understanding of how performance on tests of visual perception vary between dementia types other than between Alzheimer's Disease and various other dementias. Also, due to the variety of different tests and disease types, and the variation in statistical values reported across each study, it was not possible to conduct a meta-analysis of study results.

It is possible that the inclusion criteria and search terms used led to the exclusion of relevant studies, including studies which were not published in English or included participants with unconfirmed diagnoses of dementia. Also, the search terms used may not have captured all relevant studies, however handsearching of reference lists led to only one additional study being identified suggesting that it is unlikely that studies were missed.

Finally, although an independent rater was included only 10% of the potential studies identified by the search process were screened, and only 50% of the studies included in the review were independently reviewed for risk of bias. Ideally, all studies returned by the search process, and all studies included in the review, would have been screened and reviewed by an independent rater. However, although this was not possible within the scope of the current review, the studies which were reviewed led to 'substantial' or 'almost perfect' agreement between raters.

Areas for Future Research and Clinical Practice

The current review highlights the importance of inclusion of tests of visual perception during neuropsychological assessment. This review should prompt additional research into the nature and extent of visual perception difficulties that are associated with different forms of dementia, which may lead to more accurate and timely diagnosis for those experiencing symptoms of dementia. More accurate identification of visual problems may also increase attention to interventions to manage impairments in everyday activities. This may include, for example, adaptations to the individual's physical environment (improved lighting, pictorial signage, high contrast flooring) and regular input from occupational therapy and ophthalmology services, which can help limit the negative impact of visual difficulties on symptoms related to disorientation and confusion (Dawes et al., 2019).

It may be useful for subsequent reviews to focus on visual processing in non-Alzheimer's Disease dementias. This could help to provide a more comprehensive understanding of differential diagnosis between different dementia types. Future reviews could perhaps also focus on studies applying specific statistical measures of diagnostic accuracy, e.g., sensitivity/specificity, or specific tests of visual impairment in order for a more meaningful synthesis of results, if the evidence base in this area improves and this research becomes available.

CONCLUSION

This review provides clinically relevant information relating to how visual perception is impacted by dementia. More specifically, the review demonstrated the differences in visual perception experienced by individuals with Alzheimer's Disease and those diagnosed with other forms of dementia. The ACE-III, Clock Drawing Task and Pentagon Copy in particular appear to quickly and reliably highlight these differences. However, although significant differences in test performance between different groups were observed, the review was not

able to improve understanding of the diagnostic accuracy of these tests. It should be noted that many of these tests were included within brief screening batteries aimed at assessing various cognitive domains, and should therefore be used to prompt more detailed assessment of visual, and overall cognitive, impairment.

There is a need to improve the evidence base regarding the use of tests of visual perception for differential diagnosis in dementia, and evaluate whether accurate cut-off scores on tests of visual perception can be determined. It would be interesting to investigate whether regression models using test results from several cognitive domains, together with biomarker measures, can improve diagnostic accuracy. It is essential however that any studies aiming to improve the evidence base in this way minimise risk of bias and maintain high methodological standards, perhaps via reference to and guidance by tools such as the QUADAS-2 and STARD guidelines.

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CHAPTER 2: Major Research Project

Diagnostic Accuracy of the Visuo-spatial domain of the Addenbrooke's Cognitive Examination III

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PLAIN ENGLISH SUMMARY

Title

Diagnostic Accuracy of the Visuo-spatial domain of the Addenbrooke's Cognitive Examination III

Background

Many people diagnosed with dementia will experience some form of visual impairment, with visuo-spatial function among the most common visual process affected (Geldmecher, 2003). Accurate measurement of visuo-spatial ability is essential therefore to inform clinical judgement and may also assist with differential diagnosis and management of risk. However, the evidence base for tests of visuo-spatial ability is relatively limited. The Addenbrooke's Cognitive Examination (third edition: ACE-III; Hsieh et al, 2013) is a widely used screening tool for symptoms of neurocognitive decline, and although this includes a measure of visuo-spatial ability it is unclear how accurately this detects visuo-spatial impairment in individuals with dementia and Mild Cognitive Impairment (MCI).

Aims

The study aimed to assess how well the ACE-III detects visuo-spatial deficits in individuals with dementia and MCI. In addition, the study aimed to identify the optimal cut-off score for interpretation of ACE-III visuo-spatial performance and identification of visuo-spatial impairment.

What the study involved

The electronic health records of individuals diagnosed with dementia or MCI were accessed in order to obtain pre-existing scores on the ACE-III visuo-spatial domain. Results from other detailed neuropsychological tests of visuo-spatial function were used to assign participants to either a visual impairment (VI) group or a no impairment (NI) group. A total of 49 people were

allocated to the visual impairment group while 103 people were allocated to the no impairment group. Scores obtained by each group on the ACE-III visuo-spatial sub-test were then compared.

Results

The VI group performed significantly more poorly than the NI group on the ACE-III visuo-spatial sub-test. The ACE-III showed 'fair' diagnostic accuracy for detecting visuo-spatial impairment. The optimal cut-off score was 12.5, whereby individuals obtaining scores of 12 or below are likely to display visuo-spatial impairment.

Conclusions

The study demonstrated that the ACE-III is an adequate measure of visuo-spatial impairment in individuals with dementia and MCI. However, this should be used alongside more extensive neuropsychological assessment in cases where screening measures indicate the requirement for additional testing of dementia symptoms.

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ABSTRACT

Background: As many as 32.5% of individuals diagnosed with dementia will experience some form of visual impairment (Bowen et al, 2016), with visuo-spatial function among the most common visual process affected (Geldmecher, 2003). Reliable assessment in this area is therefore essential to accurate diagnosis. The Addenbrookes Cognitive Examination (ACE-III) is one of the most widely used screening tools in dementia assessment and includes a set of tests measuring visuo-spatial ability, with a sub-scale score ranging from 0-16. Little is known about the test's diagnostic accuracy in this specific cognitive domain. **Aims:** This study examined how well the ACE-III detects visuo-spatial impairment in individuals with dementia and Mild Cognitive Impairment (MCI). **Methods:** The electronic health records of individuals with a pre-existing diagnosis of dementia or Mild Cognitive Impairment (MCI) were accessed to obtain scores on the visuo-spatial domain of the ACE-III. Individuals were included in the study if they had completed a battery of neuropsychological tests which included assessment of visuo-spatial ability. Performance on these tests were used to allocate participants to either a visual impairment (VI) group or no impairment (NI) group. Scores on the visuo-spatial sub-test of the ACE-III were then examined to compare the VI and NI groups and determine the diagnostic accuracy of the test. **Results:** ACE-III visuo-spatial scores were significantly lower in the VI group (*n*=49; Mdn=12.0) than the NI group (*n*=103; Mdn=14.0). Receiver Operating Curve (ROC) analysis indicated 'fair' (Area Under Curve =.77) diagnostic accuracy. Scores of 12 and below are suggested as the optimal cut-off score to indicate visuo-spatial impairment, offering sensitivity and specificity values of .61 and .85. **Conclusion:** The visuo-spatial sub-test of the ACE-III is an adequate measure of visual impairment in individuals with dementia or MCI. However, this should be administered alongside additional tests of visual impairment included within more detailed neuropsychological assessment if screening measures indicate the requirement for additional testing of dementia symptoms.

Key Words: Dementia; MCI; Visuo-spatial; Visual Impairment; Addenbrookes; ACE-III

INTRODUCTION

Background

Dementia is one of the leading threats to global health and is a major cause of disability and dependence among older adults (World Health Organization, 2020). Currently, the syndrome affects as many as 46.8 million people worldwide, however this number is expected to double by 2050 (Prince et al, 2015). Between 5-8% of individuals over the age of 60 are diagnosed with dementia (World Health Organization, 2020). Women are more likely than men to be diagnosed with dementia, and it is the leading cause of death for women and second leading cause of death for men in the United Kingdom (Prince et al, 2015).

Dementia includes various symptoms which can impair a person's abilities in several cognitive domains such as memory, language, attention and executing functioning (World Health Organization, 2018). These symptoms are impacted in different ways by different forms of the syndrome, the most common of which is Alzheimer's Disease which is experienced by between 50-75% of dementia patients (Alzheimer's Society, 2020). All types of dementia, and the associated decline in cognitive function, are progressive in nature and involve shrinkage of the brain caused by cellular damage.

Almost one third of the neocortex is involved in visual processes (Van Essen and Drury, 1997). It is perhaps unsurprising therefore many individuals diagnosed with dementia experience some form of visual impairment (Bowen et al, 2016). Visual impairment can include deficits in visuo-spatial ability, defined by Simic et al. (2013) as "*processes involved in perceiving spatial location, orientation, direction and distance*" (p1119), and visuo-constructional ability, defined as "*skills needed to put together parts to form a single whole*" (Simic et al. (2013; p 1119)). Many tests aiming to assess visuo-spatial ability depend upon a combination of basic visual perception (acuity and object perception), spatial and perceptuomotor functions for successful performance. Visual impairment of any sort, but including visuo-spatial ability, can increase

the risk of falls (Fernando et al, 2017) and reduce mobility and overall quality of life (van Ooteghem et al, 2019) for individuals diagnosed with dementia or Mild Cognitive Impairment (MCI).

Accurate measurement of visuo-spatial ability is essential therefore to understand the nature of a person's difficulties and may contribute to differential diagnosis and risk management. Although several well-validated tests are available for measuring cognitive domains such as memory (Wechsler, 1987), language (Savage et al, 2013) and attention (Robertson et al, 1994) in the context of dementia, the evidence base relating to the usefulness of tests designed to assess visuo-spatial ability in people with dementia is relatively limited. The Addenbrooke's Cognitive Examination (third edition: ACE-III; Hsieh et al, 2013) is a widely used screening tool for symptoms of neurocognitive decline and includes a measure of visuo-spatial ability. However, it is unclear how accurately the visuo-spatial domain of the ACE-III detects visuo-spatial impairment in individuals with dementia and MCI.

Aims

This study aimed to assess how well the ACE-III detects visuo-spatial deficits in individuals with dementia and MCI. This was achieved by comparing the performance of individuals with and without visuo-spatial impairment on the visuo-spatial domain of the ACE-III. In addition, the study aimed to identify the optimal cut-off score for interpretation of ACE-III visuo-spatial performance and identification of visuo-spatial impairment.

METHODS

Participants

Participants included people who received a diagnosis of dementia or MCI following neuropsychological assessment from a qualified clinical psychologist based within an NHS Greater Glasgow and Clyde (NHS GG&C) Older Adult Community Mental Health Team

(OACMHT). Participants satisfied ICD-11 (WHO, 2018) criteria for diagnosis of dementia (6D80-86, 6D8Y, 6D8Z) or MCI (6D71).

Eligibility Criteria

Inclusion Criteria

In order to be included in the study, participants were required to have completed the ACE-III as part of the cognitive assessment which led to their diagnosis of dementia or MCI. In addition, at least one separate test of visuo-spatial ability must have been administered as part of a complete neuropsychological assessment. Complete neuropsychological assessment was operationalised as that involving an assessment battery utilising validated measures of cognitive domains identified in the ICD-11 (WHO, 2018) as necessary for assessment and diagnosis. This includes memory, executive functioning, attention, language, social cognition and judgement, psychomotor speed and visuo-perceptual or visuo-spatial ability.

Exclusion Criteria

Those who met the following criteria were excluded from participation in the study:

- Individuals who had an unconfirmed or unclear diagnosis of dementia or MCI
- Individuals for whom visual impairment was unknown or unclear
- Individuals with a physical impairment which may have impacted upon motor performance during tests of visuo-spatial ability (e.g., arthritis, Parkinson's Disease)
- Individuals who completed the ACE-III more than six months before or after the neuropsychological assessment
- Individuals with a diagnosis of learning/intellectual disability

Ethics

Ethical approval was granted from the West of Scotland Research Ethics Service on 5th November 2020 (REC Reference: 20/WS/0156; Appendix 2.4). Permission to proceed with the study was also provided by the local Caldicott Guardian and by the NHS GG&C Research and Innovation service.

Research was conducted by a trainee clinical psychologist under the supervision of a qualified clinical psychologist. The British Psychological Society's *'Code of Human Research Ethics'* (BPS, 2014) and '*Code of Ethics and Conduct'* (BPS, 2018) also guided the researcher's practice and ensured that safe and appropriate research principles were applied throughout the study. Recording and electronic storage of confidential patient information adhered to the Data Protection Act 2018 (UK Government, 2018), the United Kingdom's implementation of the General Data Protection Regulation (GDPR, 2018).

Recruitment Procedures

Following appropriate organisational and ethical approval, the lead author contacted all qualified clinical psychologists based across the six NHS GG&C Health and Social Care Partnership areas (East Dunbartonshire, East Renfrewshire, Inverclyde, Glasgow City, Renfrewshire, West Dunbartonshire). Clinicians were asked to provide the names and unique Clinical Health Index (CHI) numbers of all clients known to their service who satisfied the inclusion criteria and who did not violate the exclusion criteria.

Using the CHI numbers, the electronic health records of these individuals were then accessed by the lead author via the Egton Medical Information Systems (EMIS) digital health platform. Following an additional check for inclusion and exclusion criteria, relevant data for each participant was extracted from the EMIS digital health platform and recorded in a password protected Microsoft Excel database.

Justification of Sample Size

Bujang and Adnan (2016) note that sensitivity is the most appropriate measure of diagnostic utility for screening tests (over and above specificity). They provide indicators of minimum sample sizes for sensitivity analysis based on prevalence of the condition of interest in the population being sampled, and for different levels of sensitivity. Based on an estimated prevalence of visual impairment in people with dementia of 30% (Bowen et al., 2016), 45 people with visual impairment, and a total sample of 150, was proposed as a minimum sample size for determining the sensitivity if sensitivity is at least 0.8 (power of 0.826, p=0.0034).

A sample of 45 people with impairment and 105 without would have 90% power to detect a difference of d=0.76 in an independent samples t-test. In order for the ACE-III to effectively detect differences between the visual impairment (VI) and no impairment (NI) groups, and for clinicians to be confident in the clinical accuracy of these results, a large (d=0.8) effect size for this separation would be required ($p<0.05$, two-tailed).

Between April 2019 and March 2020, 2,187 individuals were diagnosed with dementia or MCI across NHS GG&C. Following discussions with members of a local OACMHT, it was estimated that around 3% of these individuals were likely to have undergone neuropsychological assessment. Therefore, approximately 66 individuals would be expected to receive a neuropsychological assessment per year, and around 528 in the 8 years the ACE-III has been used within NHS GG&C. As such, it was expected that obtaining the required sample size would have been realistic within the timeline proposed.

Measures

The visuo-spatial sub-test of the ACE-III represented the dependent variable of the study. In this test, individuals complete five tasks which rely on visuo-spatial abilities. These include a clock drawing task, copying two diagrams (infinity diagram and wire cube), dot counting and

fragmented letter identification. Scores on each sub-test are summed to produce a sub-scale score that can range from 0–16.

The independent variable, i.e., allocation to the VI or NI group, was determined by performance on visuo-spatial tests included in participant's full neuropsychological assessment batteries. If performance on at least one test of visuo-spatial ability fell within the bottom fifth percentile (or, Z-Score <-1.67; T-Score<33; Scaled Score<5: Standard Score<75), participants were allocated to the VI group. Some common neuropsychological assessments used within NHS GG&C include, among others, the Repeatable Battery for the Assessment of Neuropsychological Status (RBANS; Randolph, 2012), the Mini-Mental State Exam (MMSE; Folstein et al, 1975) and the Severe Impairment Battery (SIB; Saxton et al, 1990), each of which include measures of visuo-spatial ability.

Demographic factors including age and gender were also recorded, as was dementia type. Postcodes were used to determine socio-demographic information based on Scottish Index of Multiple Deprivation (SIMD) rank and decile.

Design and Procedure

A between-groups observational design was used in order to determine how accurately the ACE-III can identify visuo-spatial impairment. The study utilised existing data from neuropsychological assessments, and as such there was no requirement for face-to-face contact with participants or direct assessment.

Once potential participants had been identified, relevant data was recorded on a password protected Microsoft Excel database and stored on a secure NHS file drive. An anonymised data set was created for analysis using study ID pseudonyms, and postcodes were removed and replaced with relevant SIMD rank and decile values.

Data Analysis

The statistics package IBM® SPSS (version 27.0) was used to analyse the results of the study. The Shapiro-Wilk test revealed that age was normally distributed, however all other data items deviated from normal distribution. Appropriate non-parametric tests (Mann Whitney U-test) were used to examine differences between the VI and NI groups for ACE-III visuo-spatial score, SIMD Decile and SIMD Rank, while age was analysed using an Independent Samples t-test. A Chi-square test for independence was used to explore gender-based differences between each group, and statistical values, significance level and effect sizes are presented for the overall sample as well as for sub-groups based on dementia type.

Diagnostic accuracy was determined using Receiver Operating Characteristic (ROC) curve analysis and the Sensitivity, Specificity, Youden Index, Likelihood Ratios, Positive Predictive Values and Negative Predictive Values were calculated for various cut-off scores.

RESULTS

Preliminary Analyses

The study included 49 participants in the visual impairment (VI) group and 103 participants in the no impairment (NI) group. Preliminary analyses using the Shapiro Wilks Test found that age was normally distributed in the VI group (W=.967, p=.182) and NI group (W=.982, p=.187). However, for both the VI and NI groups ACE-III Visuo-spatial scores (W=.952, p=.046; W=.852, p<.001), SIMD Decile (W=.848, p<.001; W=.861, p<.001) and SIMD Rank (W=.878, p<.001; W=.892, p<.001) significantly deviated from normal. Therefore, analyses for age were investigated using parametric analysis while ACE-III Visuo-spatial scores, SIMD Decile and SIMD Rank were analysed using non-parametric tests.

Demographic Characteristics and Test Performance

Details of participant demographics and test performance for each group is outlined in Table 7 (below). This includes information on gender and mean, median, standard deviation, interquartile range and range relating to age, SIMD Decile, SIMD Rank and ACE-III Visuo-spatial scores.

Table 7: Demographic characteristics and test performance for VI and NI groups and total

		Total	Visual Impairment (N=49)	No Impairment (N=103)	Statistical Value	*p*	Effect Size
Male (%)		71 (46.7)	20 (40.8)	51 (49.5)	$\chi^2(1, n=152)=.69$, $p=.41$		
Age	Mean ± SD (Range)	71.7 ± 7.4 (54-90)	72.3 ± 8.1 (54-90)	71.5 ± 7.1 (55-87)	t(150)=.62	.54	d=.11
SIMD Decile	Mean ± SD (Range)	4.1 ± 3.1 (1-10)	4.5 ± 3.3 (1-10)	4.0 ± 2.9 (1-10)	z=-.53	.59	r=.04
	Median (IQR)	3.0 (6.0)	4.0 (6.5)	3.0 (9.0)			
SIMD Rank	Mean ± SD (Range)	2540.4 ± 2144.7 (16-6961)	2763.8 ± 2335.0 (47-6961)	2434.2 ± 2051.4 (16-6916)	z=-.52	.60	r=.04
	Median (IQR)	1913.0 (3752.0)	2495.0 (4340.5)	1804.0 (3505.0)			
ACE-III VS Score	Mean ± SD (Range)	13.0 ± 2.8 (3-16)	11.1 ± 3.3 (3-16)	14.0 ± 2.0 (7-16)	z=-5.33	<.001	r=.43
	Median (IQR)	14.0 (3.0)	12.0 (5.0)	14.0 (2.0)			

The majority of participants were female (N=81), however a Chi-square test for independence (with Yates Continuity Correction) indicated no significant association between gender and group membership, $\chi^2(1, n=152)=.69$, $p=.41$.

Similarly, an Independent Samples t-test found that the mean age of participants in the VI group (M=72.3, SD=8.1) and NI group (M=71.5, SD=7.1) did not differ significantly (t(150)=.62, *p*=.537)). SIMD Decile (Mdn=4.0, IQR=6.5) and SIMD Rank (Mdn=2495.0, IQR=4340.5) were higher in the VI group than in the NI group (Mdn=3.0, IQR=9.0: Mdn=1804.0, IQR=3505.0), but again a Mann-Whitney U Test revealed that these differences were not significant (*U*=2390.5, *z*=-.53, *p*=.59, *r*=.04; *U*=2391, *z*=-.52, *p*=.6, *r*=.04).

A significant difference between the groups for ACE-III Visuo-spatial scores was detected (*U*=1188, *z*=-5.33, *p*<.001), with scores lower in the VI group (M=11.1, SD=3.3; Mdn=12.0, IQR=5.0) than in the NI group (M=14.0, SD=2.0; Mdn=14.0, IQR=2.0). A medium-large effect size (*r*=.43) for this difference was detected. Figure 3 highlights the percentages of each score recorded in each group.

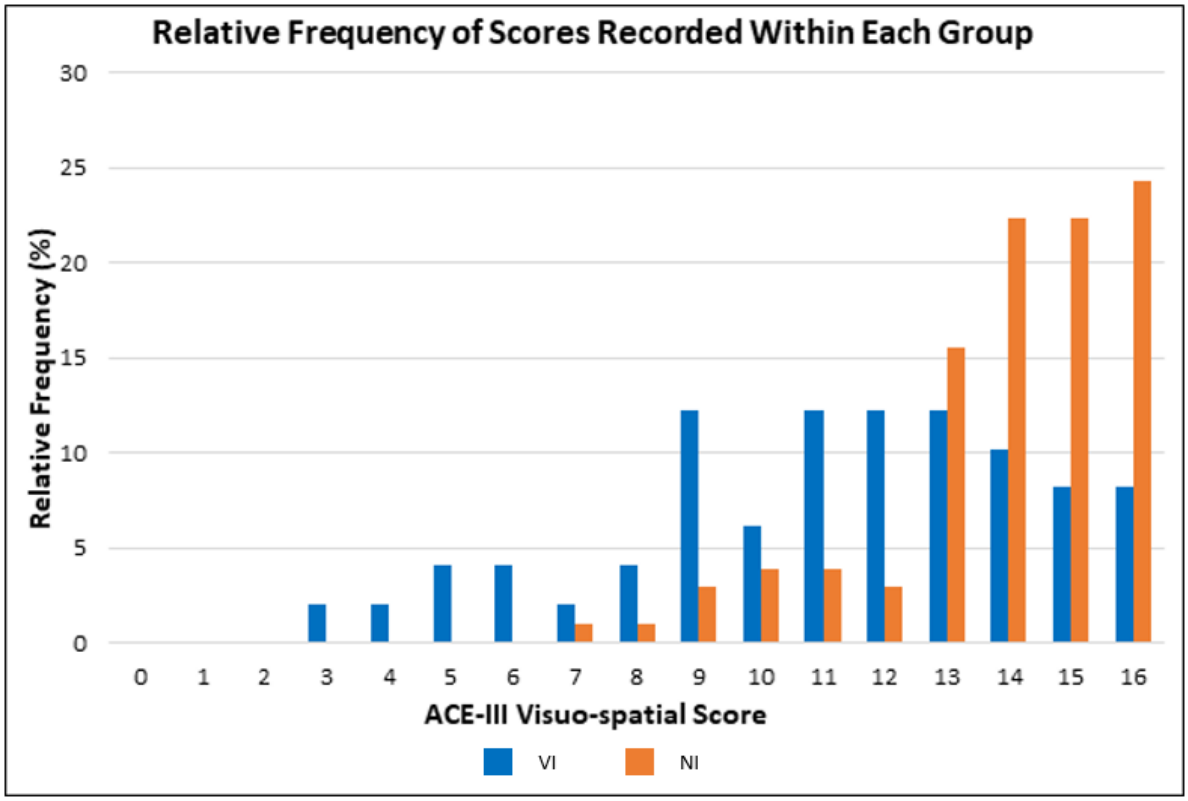

Figure 3: Relative frequency of each score recorded for Visual Impairment group and No Impairment group

This illustrates that the majority of participants in the NI group (N=87, 84.5%) obtained a score of 13 or more, while the majority of participants in the VI group (N=30, 61.2%) obtained a score below 13.

Diagnostic Utility

Receiver Operating Characteristic (ROC) curve analysis was completed to determine the optimal cut-off score for the Visuo-spatial sub-test of ACE-III. Figure 4 displays the ROC curve for ACE-III Visuo-spatial score differentiating the VI from NI groups. The Area Under the Curve (AUC; .77, 95% C.I.=.68 - .85) indicated 'fair' diagnostic accuracy.

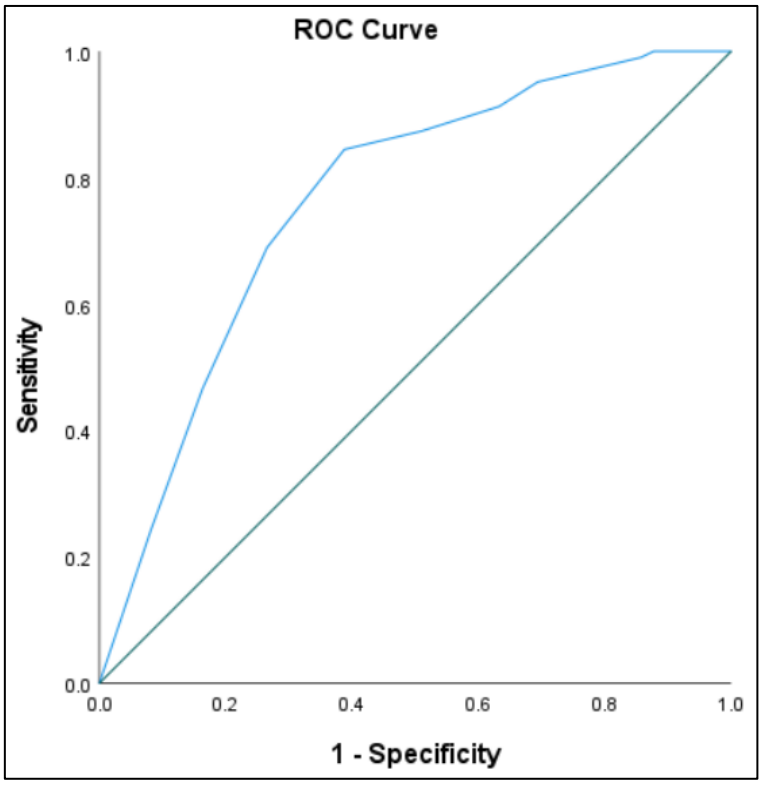

Figure 4: ROC Curve of ACE-III Visuo-spatial test detecting visual impairment

In order to determine the optimal cut-off score for detecting the presence of visuo-spatial impairment, the sensitivity, specificity, Youden Index, Likelihood Ratios (LR+; LR-) and positive and negative predictive values (PPV; NPV) were obtained. These values are presented in Table 8.

Table 8: Sensitivity, Specificity, Youden Index, Likelihood Ratios (LR+; LR-) Positive Predictive Values (PPV) and Negative Predictive Values (NPV) for the ACE-III Visuo-spatial test at different cut-off scores for visual impairment

Cut-off*	Sensitivity	Specificity	Youden Index	+LR	-LR	PPV (%)	NPV (%)
15.5	.92	.24	.16	1.21	.33	36.6	86.2
14.5	.84	.47	.31	1.58	.34	42.7	85.7
13.5	.74	.69	.43	2.39	.38	52.9	84.5
12.5	**.61**	**.85**	**.46**	**4.07**	**.46**	**65.2**	**82.1**
11.5	.49	.87	.36	3.77	.59	64.9	78.3
10.5	.37	.91	.28	4.11	.69	66.7	75.2
9.5	.31	.95	.26	6.20	.73	75.0	74.2
8.5	.18	.98	.16	9.00	.84	81.8	71.6
7.5	.14	.99	.13	14.00	.87	87.5	70.8
6.5	.12	1.00	.12	∞	.88	100	70.5
5.5	.08	1.00	.08	∞	.92	100	69.6
4.5	.04	1.00	.04	∞	.96	100	68.7
3.5	.02	1.00	.02	∞	.98	100	68.2

***** *ACE-III scores include whole values only; decimal values used for illustration*

Table 8 indicates that if one uses the maximum Youden's J score to define the optimal cut-off, then an ACE-III Visuo-spatial cut-off score should be 12.5, i.e., scores of 12 and below indicate visual impairment and scores of 13 and above to indicate no impairment. This gives a True Positive Rate (TPR - Sensitivity) of 61% and a True Negative Rate (TNR - Specificity) of 85%, as well as Likelihood Ratios of +LR=4.07 and -LR=.46. Individuals achieving a score of 12 or less would have a 65.2% chance of their Visuo-spatial impairment diagnosis being correct, while those scoring 13 or above would have an 82.1% chance of a negative test result being correct.

Disease Characteristics

Disease specific information relating to type of dementia diagnosis in each group is outlined in Table 9 (below).

Table 9: Prevalence of dementia types in Visual Impairment (VI) group, No Impairment (NI) group and overall, and percentages within disease groups

Dementia Type	VI			NI			Total
	N	% of overall VI total	% of disease group	N	% of overall NI total	% of disease group	(% of overall participants)
Mild Cognitive Impairment (MCI)	13	26.5	20.3	51	49.5	79.7	64 (42.1)
Alzheimer's Disease (AD)	14	28.6	40.0	21	20.4	60.0	35 (23.0)
Vascular Dementia (VD)	6	12.2	27.3	16	15.5	72.7	22 (14.5)
Frontotemporal Dementia (FTD)*	8	16.3	57.1	6	5.8	42.9	14 (9.2)
Mixed: AD & VD	4	8.2	44.4	5	4.9	55.6	9 (5.9)
Mixed: AD & FTD	2	4.1	100.0	0	0.0	0.0	2 (1.3)
Mixed: FTD & VD	0	0.0	0.0	2	1.9	100.0	2 (1.3)
Dementia with Lewy Bodies (DLB)	0	0.0	0.0	1	1.0	100.0	1 (0.7)
Posterior Cortical Atrophy (PCA)	1	2.0	100.0	0	0.0	0.0	1 (0.7)
Parkinson's Disease Dementia (PDD)	1	2.0	100.0	0	0.0	0.0	1 (0.7)
Unspecified	0	0.0	0.0	1	1.0	100.0	1 (0.7)

**Includes those diagnosed with Behavioural Variant FTD (bvFTD) and Primary Progressive Aphasia (PPA)*

As Figure 5 highlights, the most common diagnosis overall was MCI (42.1%). This was also the most common diagnosis within the NI group, accounting for almost half (49.5%) of all diagnoses and was the second most common diagnosis within the VI group (26.5%). Alzheimer's Disease was the most common diagnosis in the VI group (28.6%) and second

most common overall (23.0%) and in the NI group (20.4%), followed by Vascular Dementia which accounted for 14.5% of overall diagnoses.

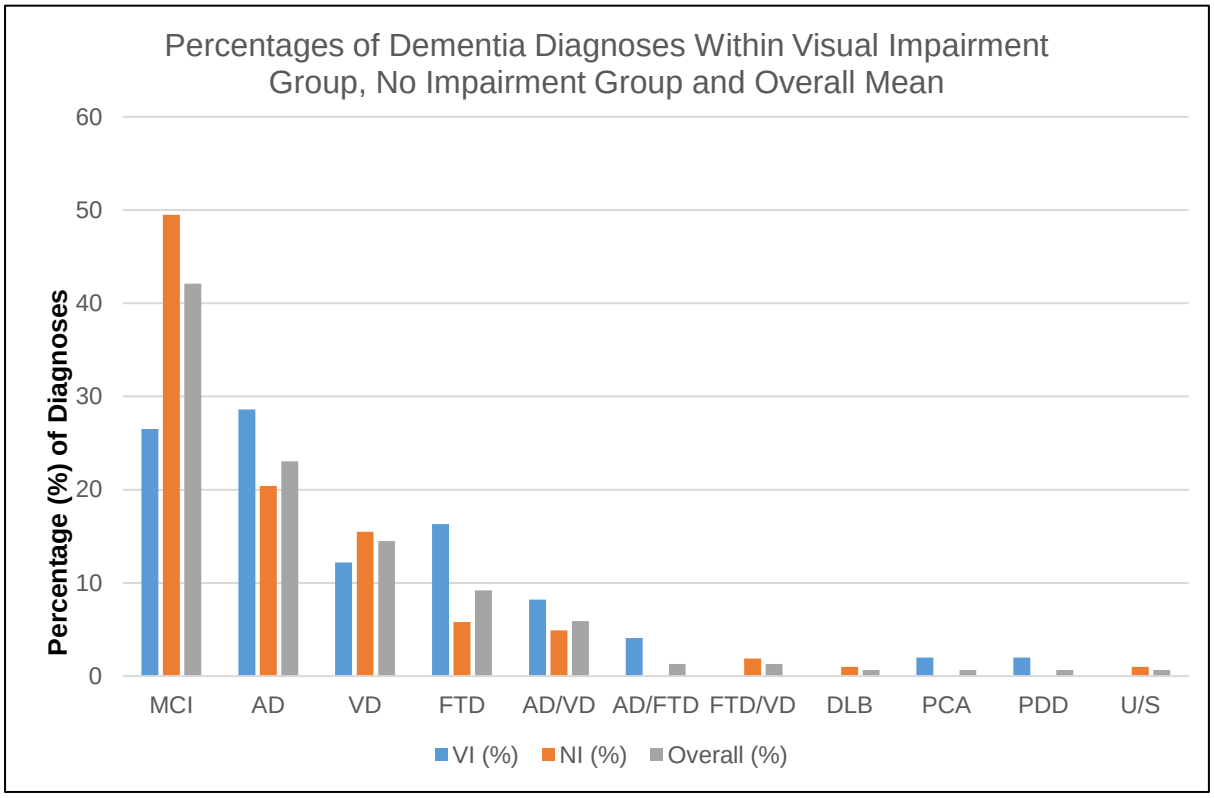

Figure 5: Percentages of dementia diagnoses within Visual Impairment group, No Impairment group and Total

Differences within each dementia 'type' between the VI group and NI group were also analysed. Table 10 highlights the demographic and test characteristics for each dementia 'type' which included more than three participants.

Table 10: Demographic and ACE-III VS scores for each dementia type

Dementia Type	Within diagnosis characteristics		Visual Impairment Group	No Impairment Group	Total	Statistical Value	*p*	Effect size
Alzheimer's Disease	N (%)		14 (40.0)	21 (60.0)	35 (100.0)			
	Male (%)		6 (42.9)	7 (33.3)	13 (37.1)	X2(1, n=35) = .05	0.83	phi =.01
	Age	M, +- SD, (Range)	71.7 +- 9.0 (54 - 85)	71.7 + -6.4 (61 - 84)	71.7 +- 7.4 (54 - 85)	t(33) = .00	1.00	d = .00
	SIMD Decile	Mdn, IQR (Range)	1.5, 4.3 (1 - 8)	3.0, 5.0 (1 - 9)	3.0, 6.0 (1 - 9)	z = -1.63	.10	r = .28
	SIMD Rank	Mdn, IQR (Range)	725.0, 2901.8 (385 - 5518)	1503.0, 3589.0 (42 - 6180)	1443.0, 3640.0 (42 - 6180)	z = -1.55	.12	r = .26
	ACE III Score	Mdn, IQR (Range)	12.0, 3.0 (6 - 16)	15.0, 2.0 (10 - 16)	14.0, 3.0 (6 - 16)	z = -3.09	**.002** (Significant)	r = .52
Frontotemporal Dementia	N (%)		8 (57.1)	6 (42.9)	14 (100.0)			
	Male (%)		3 (37.5)	4 (66.7)	7 (50.0)	X2 (1, n=14) = .29	.59	phi= .29
	Age	Mdn, IQR (Range)	76.5, 13.5 (62 - 82)	67.0, 9.0 (55 - 70)	69.5, 13.5 (55 - 82)	z = -2.01	**.05** (Significant)	r = .54
	SIMD Decile	Mdn, IQR (Range)	6.5, 8.8 (1 - 10)	5.5, 6.5 (1 - 9)	6.5, 8.0 (1-10)	z = -.20	.84	r = .05
	SIMD Rank	Mdn, IQR (Range)	4357.0, 5916.3 (47 - 6466)	3520.5, 4371.3 (647 - 5667)	4286.5, 5192.5 (47 - 6466)	z = -.13	.90	r = .03
	ACE III Score	Mdn, IQR (Range)	9.0, 3.5 (5 - 13)	12, 4.3 (8 - 16)	10.0, 5.0 (5 - 16)	z = -1.63	.10	r = .44

Dementia Type	Within diagnosis characteristics		Visual Impairment Group	No Impairment Group	Total	Statistical Value	*p*	Effect size
Mild Cognitive Impairment	N (%)		13 (20.3)	51 (79.7)	64 (100.0)			
	Male (%)		4 (30.8)	24 (47.1)	28 (43.8)	X2 (1, n = 64) = .55	.46	phi = .13
	Age	M, +- SD, (Range)	71.5 +- 8.6 (55 - 90)	71.9 +- 7.2 (56 - 87)	71.9 +- 7.4 (55 - 90)	t(62) = .174	.87	d = .05
	SIMD Decile	Mdn, IQR (Range)	5.0, 7.0 (1 - 10)	4.0, 5.0 (1 - 10)	4.0, 6.0 (1 - 10)	z = -.85	.40	r = .11
	SIMD Rank	Mdn, IQR (Range)	3350.0, 5074.0 (57 - 6758)	2485, 3433.0 (16 - 6916)	2485.0, 3919.5 (16 - 6916)	z = -.63	.53	r = .08
	ACE III Score	Mdn, IQR (Range)	13.0, 5.0 (4 - 16)	14.0, 2.0 (9 - 16)	14.0, 2.0 (4 - 16)	z = -2.07	**.04** (Significant)	r = .26
Mixed: AD & VD	N		4 (44.4)	5 (55.6)	9 (100.0)			
	Male (%)		2 (50.0)	4 (80.0)	6 (66.7)	X2(1, n=9) = .06	.81	phi = .32
	Age	Mdn, IQR (Range)	79.5, 11.5 (65 - 80)	73.0, 18.5 (59 - 79)	78.0, 15.0 (59 - 80)	z = -1.61	.11	r = .54
	SIMD Decile	Mdn, IQR (Range)	7.0, 5.3 (3 -10)	3.0, 6.5 (1 - 10)	6.0, 6.0 (1 - 10)	z = -1.21	.29	r = .41
	SIMD Rank	Mdn, IQR (Range)	4390.5, 3920.3 (1841 - 6961)	1804.0, 4420.5 (669 - 6777)	4127.0, 4065.0 (669 - 6961)	z = -1.47	.19	r = .49
	ACE III Score	Mdn, IQR (Range)	14.0, 7.8 (7 - 16)	16.0, 3.5 (10 - 16)	16.0, 5.0 (7 - 16)	z = -.54	.73	r = .18
Vascular Dementia	N		6 (27.2)	16 (72.7)	22 (100.0)			
	Male (%)		1 (16.7)	10 (62.5)	11 (50.0)	X2(1, n=22) = 2.06	.15	phi = .41
	Age	Mdn, IQR (Range)	73.5, 9.5 (59 - 79)	73.0, 14.8 (62 - 82)	73.0, 12.0 (59 - 82)	z = -.26	.80	r = .06
	SIMD Decile	Mdn, IQR (Range)	3.0, 4.5 (1 - 7)	1.5, 1.0 (1 - 6)	2.0, 1.3 (1 - 7)	z = -1.34	.18	r = .29
	SIMD Rank	Mdn, IQR (Range)	1749.5, 3354.0 (92 - 4382)	633.0, 818.5 (42 - 4149)	766.5, 1203.25 (42 - 4382)	z = -.89	.38	r = .19
	ACE III Score	Mdn, IQR (Range)	11.0, 3.5 (9 - 14)	14, 3.3 (7 - 16)	13.5, 3.3 (7 - 16)	z = -1.88	.06	r = .40

As Table 10 illustrates, the only significant differences in ACE-III scores identified between the VI and NI groups within dementia type was in the Alzheimer's Disease (AD) and Mild Cognitive Impairment (MCI) groups. Within each, those in the VI group obtained significantly lower scores (AD: *U*=56.5, *z*=-3.09, *p*=.002, *r*=.52; MCI: *U*=210.0, *z*=-.207, *p*=.04, *r*=.26), with large and small-medium effect sizes detected for these differences, respectively. Also, the median age of individuals diagnosed with Frontotemporal Dementia in the VI group was higher (Mdn=76.5, IQR=13.5) than those in the NI group (Mdn=67.0, IQR=9.0). This difference approached significance (*U*=8.5, *z*=-2.01, *p*=.05, *r*=.54) with a large effect size.

Similarly, although medium effect sizes between the VI and NI groups were detected for ACE-III scores in those diagnosed with Frontotemporal Dementia (*r*=.44) and Vascular Dementia (*r*=.40), the samples in these disease groups were too small to obtain a significant value, despite a *p* value approaching significance (p=.06) for the latter sample.

DISCUSSION

The study found that, for individuals diagnosed with dementia or MCI, the ACE-III visuo-spatial sub-test displays 'fair' diagnostic accuracy for differentiating between individuals with and without visuo-spatial impairment. Those with visuo-spatial impairment performed significantly worse on this test than those with no visuo-spatial impairment, and a medium-large effect size for the difference between these groups was identified.

A score of 12.5 is suggested as the optimal cut-off score for classification of visuo-spatial /no visuo-spatial impairment. This would offer a True Positive Rate (Sensitivity) of .61 and a True Negative Rate (Specificity) of .85, meaning that 61% of individuals with visuo-spatial impairment would be correctly classified as such. Individuals who have no visuo-spatial impairment would be correctly classified in 85% of cases.

However, it is worth considering Bujang and Adnan's (2016) assertion that sensitivity, over and above specificity, is the most appropriate measure of diagnostic utility for screening tests. Applying a cut-off score of 13.5 would increase sensitivity to .74, ensuring that 74% of individuals with a visuo-spatial impairment would be correctly classified. However, this would also increase the false positive rate from 15% to 31%.

Clinicians should therefore consider clinical priorities and implications when interpreting these scores. Applying a higher cut-off threshold would reduce the likelihood that visuo-spatial difficulties are missed, yet this would also lead to a higher rate of false positives. However, these would perhaps be identified and corrected after follow-up visuo-spatial testing as part of more comprehensive neuropsychological assessment. This emphasises the importance of utilising the ACE-III as a screening tool to determine whether more detailed assessment is required, as opposed to its use as a standalone instrument for diagnosis of dementia, or in this case detection of visuo-spatial difficulties. The modest sensitivity highlights the importance of clinicians considering carefully the patient's history and reports from patient or significant others regarding everyday difficulties that suggest the presence of visuo-spatial dysfunction. The presence of such difficulties should trigger more detailed investigation of visuo-spatial functions, even if a patient scores above the cut-off on the ACE visuo-spatial score.

The study supported the finding by Bowen et al (2016) that 32.5% of individuals with dementia display some form of visual impairment, with 32.2% of participants being allocated to the VI group. No significant differences in SIMD rank or decile were identified between the VI and NI groups, suggesting that social deprivation is not associated with increased risk of visuo-spatial impairment. However, levels of deprivation were higher for the NI group, and this effect was also observed when analysing the Frontotemporal, MCI, Mixed Dementia and Vascular Dementia groups separately. Again, it may be the

case that the sample sizes were too small to detect significant differences in SIMD rank and decile values between the VI and NI groups.

When analysing group differences based on dementia type, the VI group performed worse on the ACE-III visuo-spatial sub-test across all disease types. However, significant differences were only detected in the Alzheimer's Disease and MCI groups.

The most common diagnosis recorded was MCI, with 64 (42.1%) participants receiving this diagnosis. When analysing dementia types only, in line with prevalence rates reported elsewhere (Alzheimer's Society, 2020), Alzheimer's Disease (39.8%) and Vascular Dementia (25%) were the first and second most common dementia. However, although Dementia with Lewy Bodies and Frontotemporal Dementia are reported to typically affect 10-15% and 2% of dementia patients respectively, only one participant (1.1%) received this former diagnosis while 15.9% of participants with dementia were reported to have Frontotemporal Dementia. This observation is perhaps influenced by referral pathways within NHS GG&C, wherein patients experiencing symptoms of Dementia with Lewy Bodies may be more likely to be referred to neurology due to overlapping symptoms with Parkinson's Disease, including problems with movement and visual hallucinations (Jellinger, 2018). Those with Frontotemporal dementia however often exhibit more behavioural features, including changes in personality and social interaction (Benussi et al., 2021), and are therefore more likely to be referred to psychology services for neuropsychological assessment.

Strengths and Limitations

The study successfully obtained the required sample size indicated in the power analysis. This included participants from a variety of socio-demographic backgrounds, reflected by the wide range of SIMD decile (1-10) and rank (16-6961) values. However, this was drawn from a predominantly urban population and included only those referred

to older adult psychology services. Many individuals with dementia may receive their diagnosis from primary care services, neurology or geriatricians, and the sample may therefore not be wholly representative of individuals with dementia. Also, the study design did not enable recording of factors such as ethnicity, disability, education, employment or pre-morbid mental or physical health factors.

Also, although disease type was recorded and helped to provide some useful insight into how visuo-spatial impairment impacts different types of dementia, the sample sizes were insufficient to detect any significant disease-specific effects. As the study was observational in design it was not possible to include a control group. In the absence of COVID-19 restrictions the researcher would have been able to administer the ACE-III and additional neuropsychological assessment prospectively with participants and include a control group. This could also have enabled disease severity/stage of illness to have been controlled for, and data relating to age of onset could have been collected. In addition, a detailed and comprehensive assessment of visuo-spatial ability could have been used to determine the presence or absence of visuo-spatial impairment. The visuo-spatial assessment battery proposed by de Vries et al. (2018), for example, could have ensured the standardisation of measures used for group allocation.

Finally, although all measures were administered by qualified clinical psychologists, or by trainee clinical psychologists under the supervision of qualified clinical psychologists, there may be variability in how these measures were administered and interpreted. While the use of different examiners and assessments may have introduced extraneous variables into the study, using existing data perhaps reduced the risk of expectancy effects and demand characteristics. This may also have ensured that the results are more representative of, and generalisable to, clinical settings.

Areas for Future Research

Future research could aim to include larger sample sizes of various dementia types in order to improve understanding of the diagnostic accuracy of the ACE-III visuo-spatial sub-test across different diseases. This research could, in addition, improve understanding of how visuo-spatial impairment differs between these dementia types.

It may also be beneficial to examine the diagnostic accuracy of individual items within the ACE-III visuo-spatial sub-test. This could help to determine whether the overall accuracy could be improved by, for example, improving any tasks which fail to significantly differentiate between visually impaired and non-visually impaired groups, or whether individuals with particular diagnoses frequently display floor or ceiling effects on particular items.

Finally, replication of this study using prospective data and inclusion of a control group may enable researchers to capture more accurate information relating to ethnicity, disability, education, employment and pre-morbid mental or physical health factors. This could, for example, improve understanding of how different dementia types impact individuals from Black, Asian and Minority Ethnic (BAME) backgrounds and whether wider societal and health inequalities influence referrals and patient demographics observed within public health services.

CONCLUSION

The study provides evidence that the ACE-III Visuo-spatial domain detects the presence of visuo-spatial impairment with fair accuracy at a cut-off of 12.5. However, clinicians must also pay close attention to patient history, and to contemporary accounts and observations regarding everyday visuo-spatial functions, in order to determine if more detailed investigation of visuo-spatial ability are required. These findings should be of

benefit to clinicians by improving the accuracy of neuropsychological assessment, which in turn should help to ensure individuals experiencing cognitive decline receive timely and definitive diagnosis.

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SYSTEMATIC REVIEW APPENDICES (CHAPTER 1)

Appendix 1.1 – Manuscript Submission Guidelines: Journal of Geriatric Psychiatry and Neurology (Sections 1 and 2; Full submission guidelines available at https://journals.sagepub.com/author-instructions/JGP)

Manuscript Submission Guidelines:

Manuscript Submission Guidelines: *Journal of Geriatric Psychiatry and Neurology*

This Journal is a member of the Committee on Publication Ethics

This Journal recommends that authors follow the Recommendations for the Conduct, Reporting, Editing, and Publication of Scholarly Work in Medical Journals formulated by the International Committee of Medical Journal Editors (ICMJE).

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1. What do we publish?

1.1 Aims & Scope

1.2 General Instructions

1.3 Writing your paper

2. Editorial policies

2.1 Peer review policy

2.2 Authorship

2.3 Acknowledgements

2.4 Funding

2.5 Declaration of conflicting interests

2.6 Research ethics and patient consent

2.7 Clinical trials

2.8 Reporting guidelines

2.9 Research Data

3. Publishing policies

1. What do we publish?

1.1 Aims & Scope

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1.2 General Instructions

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All material (abstracts, keywords, text, tables, and figure captions) should be typed double-spaced. Computer preparation is mandatory. Subheading should be used to designate the different sections of the text. References should be numbered consecutively throughout the text. Provide a list of three to six keywords to assist indexing of the article.

Articles of any length are considered.

Title page: The title should be brief and meaningful. The authors' first and last names, academic or medical degrees, and affiliations should follow the title.

Authorship should be limited to direct participants, although technical assistance can be acknowledged as a footnote. A separate paragraph should identify where the work was done, if supported by a grant or otherwise, and the meeting, if any, at which the paper was presented.

Abstract: An abstract of approximately 150 words should be provided on. This abstract should be factual and should present the reason for the study, the main findings, and the principal conclusions.

Text: This should follow the usual format for scientific articles. Pages should be numbered consecutively. All abbreviations should be spelled out at first mention. Only generic names of drugs should be used.

Figures and tables: Special care should be given to the preparation of figures and tables, including captions and explanatory information. Technical excellence is stressed. Lettering and arrows, where applicable, should be done in a professional manner. Color illustrations are unacceptable for publication without prior permission of the publisher. Recognizable photographs of patients must be masked and must carry with them written permission for publication. Captions for all figures should be typewritten double-spaced, with numbers corresponding to those on the figures themselves.

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reference list. Such citations may be noted in the text. Some basic information regarding references and the reference list has been listed below.

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Basic rules for the reference list:

- The title “References” is centered at the top of a separate page at the end of the document.
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- The reference list should be single-spaced. Single-space between entries.
- The second line and all subsequent lines of each item in the reference list should be indented (hanging indent).
- Do not use “et al.” in the Reference list at the end; names of all authors of a publication should be listed there.

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- **Books Author(s) separated by commas.**
    - ***Title of Book.*** **Place of publication: Publisher; year.**
    - Goldberg L, Elliot DL. *Exercise for Prevention and Treatment of Illness*. Philadelphia, Pa: FA Davis Co; 1994.
- **Edited book.**
    - **Author(s), eds. *Title of Book.* Place of publication: Publisher; year.**
    - Armitage JO, Antman KH, eds. *High Dose Cancer Therapy: Pharmacology, Hematopoietins, Stem Cells*. Baltimore, Md: Williams & Wilkins; 1995.
- **Chapter or article from a book Author(s) of article.**
    - **Title of article. In: Editor's name, ed. *Title of Book*. Place of publication: Publisher; Year: Chapter or page number.**
    - Gamble VN. On becoming a physician: a dream not deferred. In: White EC, ed. *The Black Women's Health Book: Speaking for Ourselves*. Seattle, Wash: Seal Press; 1990:52-64.
- **Articles in journals**
    - AMA style requires the use of standard abbreviations for all references, when applicable. Abbreviations for many common medical journals can

be found in the AMA Manual of Style (pp.473-479). Additional abbreviations can be searched in the PubMed Journal Database (http://www.ncbi.nlm.nih.gov/nlmcatalog/journalbs).

- **One author** (do not include issue number or month unless volumes are not consecutively numbered)
    - Author. Article title. *Journal Title.* Month Year;Volume:Inclusive page numbers.
    - Angelo J. A survey of persons who use integrated control devices. *Assist Technol*. 1998;10:77-83.
- **Articles in Online Journals**
    - The preferred citation style for an electronic journal uses a DOI (digital object identifier). The DOI provides a persistent link to the electronic item and is considered to be more stable than a URL. If the DOI is not given on the full text article or in the citation, use a DOI lookup tool to locate it (http://www.crossref.org/guestquery/) or use the format for an article without a DOI.
- **Article from online journals with DOI available.** Note that when using a DOI, no access date or URL are used.
    - **Author. Title of article. *Name of Journal*. Year;vol(issue):pages. doi:xx.xxxx.**
    - Florez HR, Martinez RL. Outdoor exercise reduces the risk of hypovitaminosis D in the obese. *J Steroid Biochem Mol Bio.* 2007;103(3-5):679-681. doi:10.1016 /j.jsbmb.2006.12.032.
- **Article from online journals without DOI available**. The accessed date will often be the only date available.
    - **Author. Title of article. *Name of Journal*. Year;vol(issue);pages. URL. Published date. Updated date. Accessed date.**
    - Hay PJ. Understanding bulimia. *Aust Fam Physician*. 2007;36(9):708-712. http://www.racgp.org.au/afp/200709/18554. Accessed October 11, 2009.
- **Web pages**
    - **Author or responsible body. Title of item cited. Name of website. URL. Published date. Updated date. Accessed date.**
    - World Health Organization. Saving the future generation in Darfur. World Health

Organization. http://www.who.int/features/2007/child_health/en/index.html. Published July 7, 2007. Accessed October 11, 2009.

- **Other Media.** Use for DVDs, videos, cd-roms, and other media formats.
    - **Author. Title [format]. Publisher place: Publisher; Year.**
    - Holzknect J. *History of physical therapy in the United States* [DVD]. New York, NY: Insight Media; 2007.

IMPORTANT NOTE: To encourage a faster production process of your article, you are requested to closely adhere to the points above for references. Otherwise, it will entail a long process of solving copyeditor's queries and may directly affect the publication time of your article. In case of any question, please contact the journal editor at James.M.Ellison@ChristianaCare.org.

1.3 Writing your paper

The SAGE Author Gateway has some general advice and on how to get published, plus links to further resources.

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2. Editorial policies

2.1 Peer review policy

Journal of Geriatric Psychiatry and Neurology operates a conventional single-blind reviewing policy in which the reviewer's name is always concealed from the submitting author.

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2.2 Authorship

Papers should only be submitted for consideration once consent is given by all contributing authors. Those submitting papers should carefully check that all those whose work contributed to the paper are acknowledged as contributing authors.

The list of authors should include all those who can legitimately claim authorship. This is all those who:

(i) Made a substantial contribution to the concept or design of the work; or acquisition, analysis or interpretation of data,

(ii) Drafted the article or revised it critically for important intellectual content,

(iii) Approved the version to be published,

(iv) Each author should have participated sufficiently in the work to take public responsibility for appropriate portions of the content.

Authors should meet the conditions of all of the points above. When a large, multicentre group has conducted the work, the group should identify the individuals who accept direct responsibility for the manuscript. These individuals should fully meet the criteria for authorship.

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All contributors who do not meet the criteria for authorship should be listed in an Acknowledgements section. Examples of those who might be acknowledged include a person who provided purely technical help, or a department chair who provided only general support.

Any acknowledgements should appear first at the end of your article prior to your Declaration of Conflicting Interests (if applicable), any notes and your References.

2.3.1 Third party submissions

Where an individual who is not listed as an author submits a manuscript on behalf of the author(s), a statement must be included in the Acknowledgements section of the manuscript and in the accompanying cover letter. The statements must:

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- Identify any entities that paid for this assistance
- Confirm that the listed authors have authorized the submission of their manuscript via third party and approved any statements or declarations, e.g. conflicting interests, funding, etc.

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– including the individual's name, company and level of input – and identify the entity that paid for this assistance. It is not necessary to disclose use of language polishing services.

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Journal of Geriatric Psychiatry and Neurology requires all authors to acknowledge their funding in a consistent fashion under a separate heading. Please visit the Funding Acknowledgements page on the SAGE Journal Author Gateway to confirm the format of the acknowledgment text in the event of funding, or state that: This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

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It is the policy of *Journal of Geriatric Psychiatry and Neurology* to require a declaration of conflicting interests from all authors enabling a statement to be carried within the paginated pages of all published articles.

Please ensure that a 'Declaration of Conflicting Interests' statement is included at the end of your manuscript, after any acknowledgements and prior to the references. If no conflict exists, please state that 'The Author(s) declare(s) that there is no conflict of interest'. For guidance on conflict of interest statements, please see the ICMJE recommendations here

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Medical research involving human subjects must be conducted according to the World Medical Association Declaration of Helsinki

Submitted manuscripts should conform to the ICMJE Recommendations for the Conduct, Reporting, Editing, and Publication of Scholarly Work in Medical Journals, and all papers reporting animal and/or human studies must state in the methods section that the relevant Ethics Committee or Institutional Review Board provided (or waived) approval. Please ensure that you have provided the full name and institution of the review committee, in addition to the approval number.

For research articles, authors are also required to state in the methods section whether participants provided informed consent and whether the consent was written or verbal.

Information on informed consent to report individual cases or case series should be included in the manuscript text. A statement is required regarding whether written informed consent for patient information and images to be published was provided by the patient(s) or a legally authorized representative. Please do not submit the patient's actual written informed consent with your article, as this in itself breaches the patient's confidentiality. The Journal requests that you confirm to us, in writing, that you have obtained written informed consent but the written consent itself should be held by the authors/investigators themselves, for example in a patient's hospital record. The confirmatory letter may be uploaded with your submission as a separate file.

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2.8 Reporting guidelines

The relevant EQUATOR Network reporting guidelines should be followed depending on the type of study. For example, all randomized controlled trials submitted for publication should include a completed CONSORT flow chart as a

cited figure and the completed CONSORT checklist should be uploaded with your submission as a supplementary file. Systematic reviews and meta-analyses should include the completed PRISMA flow chart as a cited figure and the completed PRISMA checklist should be uploaded with your submission as a supplementary file. The EQUATOR wizard can help you identify the appropriate guideline.

Other resources can be found at NLM's Research Reporting Guidelines and Initiatives

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The journal is committed to facilitating openness, transparency and reproducibility of research, and has the following research data sharing policy. For more information, including FAQs please visit the SAGE Research Data policy pages.

Subject to appropriate ethical and legal considerations, authors are encouraged to:

- share your research data in a relevant public data repository
- include a data availability statement linking to your data. If it is not possible to share your data, we encourage you to consider using the statement to explain why it cannot be shared.
- cite this data in your research

Appendix 1.2 – Risk of Bias Tool - QUADAS-2

		Prats-Sedano et al, 2020	Pouzeta, A. et al, 2019	Salimi, S. et al, 2019	Scharre, D.W. et al, 2016	Park, L.Q. et al, 2015	Giovagnoli, A.R. et al, 2008	Kandiah, N. et al, 2009	Charles, R.F & Hillis, A.H., 2005	Tiraboschi, P. et al, 2006	Graham, N.L. et al, 2003	Ala, T.A. et al, 2001	Elfgren, C. et al, 1994	Yamamoto, E. et al, 2017	Gnanalingham, K.K. et al, 1997
PATIENT SELECTION															
Risk of Bias															
Was a consecutive or random sample of patients enrolled?	Yes/No/Unclear	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Was a case-control design avoided?	Yes/No/Unclear	No	No	No	No	No	No	No	No	No	No	No	No	No	No

Did the study avoid inappropriate exclusions?	Yes/No/Unclear	Unclear	Yes	Yes	Unclear	Yes	Unclear	Unclear	Unclear	Unclear	Yes	Unclear	Unclear	Unclear	No
Could the selection of patients have introduced bias?	Risk: Low/High/Unclear	Low	Low	Low	Low	Low	Low	Low	Low	Low	Low	High	Unclear	Low	Low
Concerns Regarding Applicability															
Is there concern that the included patients do not match the review question?	Concern: Low/High/Unclear	Low	Low	Low	Low	Low	Low	Low	Low	Low	Low	High	Low	Low	Low
INDEX TEST(S)															
Risk of Bias															
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes/No/Unclear	Yes	Yes	Yes	Unclear	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	Yes	Yes
If a threshold was used, was it pre-specified?	Yes/No/Unclear	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A

Could the conduct or interpretation of the index test have introduced bias?	Risk: Low/High/Unclear	Low	Low	Low	Low	Low	Low	Low	Low	Unclear	Low	Low	Low	High	Low
Concerns Regarding Applicability															
Is there concern that the index test, its conduct, or interpretation differ from the review question?	Concern: Low/High/Unclear	Low	Low	Low	Low	Low	Unclear	Low	Low	Unclear	Low	Low	Unclear	Unclear	Low
REFERENCE STANDARD															
Risk of Bias															
Is the reference standard likely to correctly classify the target condition?	Yes/No/Unclear	Yes	Yes	Unclear	Unclear	Yes	Unclear	Yes	Unclear	Unclear	Yes	Unclear	Unclear	Unclear	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	Yes/No/Unclear	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	Yes	Yes

Could the reference standard, its conduct, or its interpretation have introduced bias?	Risk: Low/High/Unclear	Low	Low	Low	Low	Low	Low	Low	Low	Low	Low	Low	Low	Low	Low
Concerns Regarding Applicability															
Is there concern that the target condition as defined by the reference standard does not match the review question?	Concern: Low/High/Unclear	Low	Low	Low	Low	Low	Unclear	Low	Low	Low	Low	Unclear	Low	Low	Low
FLOW AND TIMING															
Risk of Bias															
Was there an appropriate interval between index test(s) and reference standard?	Yes/No/Unclear	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	Unclear	Yes	Yes
Did all patients receive a reference standard?	Yes/No/Unclear	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	Unclear	Yes	Yes

Did patients receive the same reference standard?	Yes/No/Unclear	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Were all patients included in the analysis?	Yes/No/Unclear	Unclear	No	No	Unclear	No	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear
Could the patient flow have introduced bias?	Risk: Low/High/Unclear	Low	Low	Low	Low	Low	Low	Low	Low	Low	Low	Low	Low	Low	Low	Low

Appendix 1.3 – Quality Assessment: STARD Checklist

Section & Topic	No	Item
TITLE OR ABSTRACT		
	1	Identification as a study of diagnostic accuracy using at least one measure of accuracy (such as sensitivity, specificity, predictive values, or AUC)
ABSTRACT		
	2	Structured summary of study design, methods, results, and conclusions (for specific guidance, see STARD for Abstracts)
INTRODUCTION		
	3	Scientific and clinical background, including the intended use and clinical role of the index test
	4	Study objectives and hypotheses
METHODS		
Study design	**5**	Whether data collection was planned before the index test and reference standard were performed (prospective study) or after (retrospective study)
Participants	**6**	Eligibility criteria
	7	On what basis potentially eligible participants were identified (such as symptoms, results from previous tests, inclusion in registry)
	8	Where and when potentially eligible participants were identified (setting, location and dates)
	9	Whether participants formed a consecutive, random or convenience series
Test methods	**10a**	Index test, in sufficient detail to allow replication
	10b	Reference standard, in sufficient detail to allow replication
	11	Rationale for choosing the reference standard (if alternatives exist)
	12a	Definition of and rationale for test positivity cut-offs or result categories of the index test, distinguishing pre-specified from exploratory
	12b	Definition of and rationale for test positivity cut-offs or result categories of the reference standard, distinguishing pre-specified from exploratory
	13a	Whether clinical information and reference standard results were available to the performers/readers of the index test
	13b	Whether clinical information and index test results were available to the assessors of the reference standard
Analysis	**14**	Methods for estimating or comparing measures of diagnostic accuracy
	15	How indeterminate index test or reference standard results were handled
	16	How missing data on the index test and reference standard were handled
	17	Any analyses of variability in diagnostic accuracy, distinguishing pre-specified from exploratory
	18	Intended sample size and how it was determined
RESULTS		
Participants	**19**	Flow of participants, using a diagram
	20	Baseline demographic and clinical characteristics of participants
	21a	Distribution of severity of disease in those with the target condition
	21b	Distribution of alternative diagnoses in those without the target condition
	22	Time interval and any clinical interventions between index test and reference standard
Test results	**23**	Cross tabulation of the index test results (or their distribution) by the results of the reference standard
	24	Estimates of diagnostic accuracy and their precision (such as 95% confidence intervals)
	25	Any adverse events from performing the index test or the reference standard
DISCUSSION		
	26	Study limitations, including sources of potential bias, statistical uncertainty, and generalisability
	27	Implications for practice, including the intended use and clinical role of the index test
OTHER INFORMATION		
	28	Registration number and name of registry
	29	Where the full study protocol can be accessed
	30	Sources of funding and other support; role of funders

Appendix 1.4 – Quality Assessment: STARD Ratings

Item	Prats-Sedano et al, 2020	Pouzeta, A. et al, 2019	Salimi, S. et al, 2019	Scharre, D.W. et al, 2016	Park, L.Q. et al, 2015	Giovagnoli, A.R. et al, 2008	Kandiah, N. et al, 2009	Charles, R.F & Hillis, A.H., 2005	Tiraboschi, P. et al, 2006	Graham, N.L. et al, 2003	Ala, T.A. et al, 2001	Elfgren, C. et al, 1994	Yamamoto, E. et al, 2017	Gnanalingham, K.K. et al, 1997	Mean
1	2	1	2	2	2	2	2	2	2	1	2	2	2	2	1.9
2	2	2	2	1	1	1	2	2	1	2	2	1	1	2	1.6
3	2	2	1	1	2	2	1	2	1	2	1	1	1	1	1.4
4	2	2	2	1	2	2	2	1	1	1	1	1	1	1	1.4
5	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2.0
6	1	2	2	1	1	1	2	2	2	1	1	1	1	2	1.4
7	1	2	2	2	1	2	2	2	2	1	1	1	1	2	1.6
8	1	1	1	1	1	1	2	1	2	1	1	1	1	1	1.1
9	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2.0
10a	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2.0
10b	2	2	2	2	2	2	2	2	2	2	2	1	2	2	1.9
11	2	2	1	1	2	1	1	1	1	1	1	0	2	1	1.2
12a	0	0	0	0	1	0	1	1	0	1	1	1	1	0	0.5
12b	2	1	2	2	2	2	1	1	1	1	2	1	2	2	1.6
13a	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0.0
13b	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0.0
14	2	2	2	2	1	2	2	2	1	2	1	2	1	2	1.7
15	0	0	0	0	1	0	1	1	0	1	0	0	0	1	0.4
16	0	1	1	0	2	0	0	0	0	1	0	0	0	0	0.4
17	0	0	1	1	1	1	1	1	1	2	0	0	0	1	0.7
18	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0.0

19	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0.0
20	2	2	2	2	1	2	1	1	2	1	2	2	1	2	1.6
21a	1	1	2	2	2	2	1	1	1	1	0	0	1	1	1.1
21b	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0.1
22	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0.0
23	2	2	2	2	2	2	2	2	2	2	1	1	2	2	1.9
24	2	2	2	2	2	1	1	1	2	2	1	2	1	1	1.6
25	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0.0
26	1	1	2	1	1	0	1	1	2	2	1	0	2	1	1.1
27	2	1	1	1	1	1	1	1	2	2	1	1	1	2	1.3
Total/62	**35**	**35**	**38**	**33**	**37**	**33**	**34**	**34**	**34**	**36**	**28**	**25**	**30**	**36**	**33.4**

MAJOR RESEARCH PROJECT APPENDICES (CHAPTER 2)

Appendix 2.1 – Manuscript Submission Guidelines: Journal of Geriatric Psychiatry and Neurology (Sections 1 and 2: Full submission guidelines available at https://journals.sagepub.com/author-instructions/JGP)

Manuscript Submission Guidelines:

Manuscript Submission Guidelines: *Journal of Geriatric Psychiatry and Neurology*

This Journal is a member of the Committee on Publication Ethics

This Journal recommends that authors follow the Recommendations for the Conduct, Reporting, Editing, and Publication of Scholarly Work in Medical Journals formulated by the International Committee of Medical Journal Editors (ICMJE).

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1. What do we publish?

1.1 Aims & Scope

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2.6 Research ethics and patient consent

2.7 Clinical trials

2.8 Reporting guidelines

2.9 Research Data

3. Publishing policies

1. What do we publish?

1.1 Aims & Scope

Before submitting your manuscript to Journal of Geriatric Psychiatry and Neurology, please ensure you have read the Aims & Scope.

1.2 General Instructions

Manuscripts should be submitted electronically to https://mc.manuscriptcentral.com/jgpn. Authors will be required to set up an online account on the SageTrack system powered by ScholarOne. Manuscripts will be sent out anonymously for editorial evaluation. Obtaining permission for any quoted or reprinted material that requires permission is the responsibility of the author. Submission of a manuscript implies commitment to publish in the journal. Authors submitting manuscripts to the journal should not simultaneously submit them to another journal, nor should manuscripts have been published elsewhere in substantially similar form or with substantially similar content. Authors in doubt about what constitutes prior publication should consult the Editor: James M. Ellison, MD, MPH, James.M.Ellison@ChristianaCare.org.

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All material (abstracts, keywords, text, tables, and figure captions) should be typed double-spaced. Computer preparation is mandatory. Subheading should be used to designate the different sections of the text. References should be numbered consecutively throughout the text. Provide a list of three to six keywords to assist indexing of the article.

Articles of any length are considered.

Title page: The title should be brief and meaningful. The authors' first and last names, academic or medical degrees, and affiliations should follow the title.

Authorship should be limited to direct participants, although technical assistance can be acknowledged as a footnote. A separate paragraph should identify where the work was done, if supported by a grant or otherwise, and the meeting, if any, at which the paper was presented.

Abstract: An abstract of approximately 150 words should be provided on. This abstract should be factual and should present the reason for the study, the main findings, and the principal conclusions.

Text: This should follow the usual format for scientific articles. Pages should be numbered consecutively. All abbreviations should be spelled out at first mention. Only generic names of drugs should be used.

Figures and tables: Special care should be given to the preparation of figures and tables, including captions and explanatory information. Technical excellence is stressed. Lettering and arrows, where applicable, should be done in a professional manner. Color illustrations are unacceptable for publication without prior permission of the publisher. Recognizable photographs of patients must be masked and must carry with them written permission for publication. Captions for all figures should be typewritten double-spaced, with numbers corresponding to those on the figures themselves.

Tables should be numbered consecutively according to their in-text citation. Each should be typed double-spaced and should be no larger than a single page. Include a brief descriptive title and an indication of its position in the text.

References: Authors are responsible for correctness and completeness of references. References should be typed double-spaced on separate pages. They should be arranged according to their order of appearance in the text, and indicated by superscript numbers. References should be typed in accordance with the style shown below for book and journal articles. Up to four authors should be listed; when there are more than four, only the first three should be listed, followed by "et al." Abbreviations of journal names should conform to the style in Index Medicus. Abstracts, editorials, and letters to the editor should be noted as such. Personal communications, unpublished manuscripts submitted but not yet accepted, and similar unpublished items should not appear in the

reference list. Such citations may be noted in the text. Some basic information regarding references and the reference list has been listed below.

References List

Basic rules for the reference list:

- The title “References” is centered at the top of a separate page at the end of the document.
- Entries are preceded by their number and are given in numerical order.
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- The second line and all subsequent lines of each item in the reference list should be indented (hanging indent).
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Here are a few examples of commonly found references. For more examples please check AMA (11th Ed).

- **Books Author(s) separated by commas.**
    - ***Title of Book.* Place of publication: Publisher; year.**
    - Goldberg L, Elliot DL. *Exercise for Prevention and Treatment of Illness*. Philadelphia, Pa: FA Davis Co; 1994.
- **Edited book.**
    - **Author(s), eds. *Title of Book.* Place of publication: Publisher; year.**
    - Armitage JO, Antman KH, eds. *High Dose Cancer Therapy: Pharmacology, Hematopoietins, Stem Cells*. Baltimore, Md: Williams & Wilkins; 1995.
- **Chapter or article from a book Author(s) of article.**
    - **Title of article. In: Editor's name, ed. *Title of Book*. Place of publication: Publisher; Year: Chapter or page number.**
    - Gamble VN. On becoming a physician: a dream not deferred. In: White EC, ed. *The Black Women's Health Book: Speaking for Ourselves*. Seattle, Wash: Seal Press; 1990:52-64.
- **Articles in journals**
    - AMA style requires the use of standard abbreviations for all references, when applicable. Abbreviations for many common medical journals can

be found in the AMA Manual of Style (pp.473-479). Additional abbreviations can be searched in the PubMed Journal Database (http://www.ncbi.nlm.nih.gov/nlmcatalog/journalbs).

- **One author** (do not include issue number or month unless volumes are not consecutively numbered)
    - Author. Article title. *Journal Title.* Month Year;Volume:Inclusive page numbers.
    - Angelo J. A survey of persons who use integrated control devices. *Assist Technol*. 1998;10:77-83.
- **Articles in Online Journals**
    - The preferred citation style for an electronic journal uses a DOI (digital object identifier). The DOI provides a persistent link to the electronic item and is considered to be more stable than a URL. If the DOI is not given on the full text article or in the citation, use a DOI lookup tool to locate it (http://www.crossref.org/guestquery/) or use the format for an article without a DOI.
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    - **Author. Title of article. *Name of Journal*. Year;vol(issue):pages. doi:xx.xxxx.**
    - Florez HR, Martinez RL. Outdoor exercise reduces the risk of hypovitaminosis D in the obese. *J Steroid Biochem Mol Bio.* 2007;103(3-5):679-681. doi:10.1016 /j.jsbmb.2006.12.032.
- **Article from online journals without DOI available**. The accessed date will often be the only date available.
    - **Author. Title of article. *Name of Journal*. Year;vol(issue);pages. URL. Published date. Updated date. Accessed date.**
    - Hay PJ. Understanding bulimia. *Aust Fam Physician*. 2007;36(9):708-712. http://www.racgp.org.au/afp/200709/18554. Accessed October 11, 2009.
- **Web pages**
    - **Author or responsible body. Title of item cited. Name of website. URL. Published date. Updated date. Accessed date.**
    - World Health Organization. Saving the future generation in Darfur. World Health

Organization. http://www.who.int/features/2007/child_health/en/index.html. Published July 7, 2007. Accessed October 11, 2009.

- **Other Media.** Use for DVDs, videos, cd-roms, and other media formats.
    - **Author. Title [format]. Publisher place: Publisher; Year.**
    - Holzknect J. *History of physical therapy in the United States* [DVD]. New York, NY: Insight Media; 2007.

IMPORTANT NOTE: To encourage a faster production process of your article, you are requested to closely adhere to the points above for references. Otherwise, it will entail a long process of solving copyeditor's queries and may directly affect the publication time of your article. In case of any question, please contact the journal editor at James.M.Ellison@ChristianaCare.org.

1.3 Writing your paper

The SAGE Author Gateway has some general advice and on how to get published, plus links to further resources.

1.3.1 Make your article discoverable

For information and guidance on how to make your article more discoverable, visit our Gateway page on How to Help Readers Find Your Article Online

2. Editorial policies

2.1 Peer review policy

Journal of Geriatric Psychiatry and Neurology operates a conventional single-blind reviewing policy in which the reviewer's name is always concealed from the submitting author.

Journal of Geriatric Psychiatry and Neurology is committed to delivering high quality, fast peer-review for your paper, and as such has partnered with Publons. Publons is a third party service that seeks to track, verify and give credit for peer review. Reviewers for JGP and can opt in to Publons in order to claim their reviews or have them automatically verified and added to their

reviewer profile. Reviewers claiming credit for their review will be associated with the relevant journal, but the article name, reviewer's decision and the content of their review is not published on the site. For more information visit the Publons website.

The Editor or members of the Editorial Board may occasionally submit their own manuscripts for possible publication in the journal. In these cases, the peer review process will be managed by alternative members of the Board and the submitting Editor/Board member will have no involvement in the decision-making process.

2.2 Authorship

Papers should only be submitted for consideration once consent is given by all contributing authors. Those submitting papers should carefully check that all those whose work contributed to the paper are acknowledged as contributing authors.

The list of authors should include all those who can legitimately claim authorship. This is all those who:

(i) Made a substantial contribution to the concept or design of the work; or acquisition, analysis or interpretation of data,

(ii) Drafted the article or revised it critically for important intellectual content,

(iii) Approved the version to be published,

(iv) Each author should have participated sufficiently in the work to take public responsibility for appropriate portions of the content.

Authors should meet the conditions of all of the points above. When a large, multicentre group has conducted the work, the group should identify the individuals who accept direct responsibility for the manuscript. These individuals should fully meet the criteria for authorship.

Acquisition of funding, collection of data, or general supervision of the research group alone does not constitute authorship, although all contributors who do not meet the criteria for authorship should be listed in the Acknowledgments section. Please refer to the International Committee of Medical Journal Editors (ICMJE) authorship guidelines for more information on authorship.

2.3 Acknowledgements

All contributors who do not meet the criteria for authorship should be listed in an Acknowledgements section. Examples of those who might be acknowledged include a person who provided purely technical help, or a department chair who provided only general support.

Any acknowledgements should appear first at the end of your article prior to your Declaration of Conflicting Interests (if applicable), any notes and your References.

2.3.1 Third party submissions

Where an individual who is not listed as an author submits a manuscript on behalf of the author(s), a statement must be included in the Acknowledgements section of the manuscript and in the accompanying cover letter. The statements must:

- Disclose this type of editorial assistance – including the individual's name, company and level of input
- Identify any entities that paid for this assistance
- Confirm that the listed authors have authorized the submission of their manuscript via third party and approved any statements or declarations, e.g. conflicting interests, funding, etc.

Where appropriate, SAGE reserves the right to deny consideration to manuscripts submitted by a third party rather than by the authors themselves.

2.3.2 Writing assistance

Individuals who provided writing assistance, e.g. from a specialist communications company, do not qualify as authors and so should be included in the Acknowledgements section. Authors must disclose any writing assistance

– including the individual's name, company and level of input – and identify the entity that paid for this assistance. It is not necessary to disclose use of language polishing services.

2.4 Funding

Journal of Geriatric Psychiatry and Neurology requires all authors to acknowledge their funding in a consistent fashion under a separate heading. Please visit the Funding Acknowledgements page on the SAGE Journal Author Gateway to confirm the format of the acknowledgment text in the event of funding, or state that: This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

2.5 Declaration of conflicting interests

It is the policy of *Journal of Geriatric Psychiatry and Neurology* to require a declaration of conflicting interests from all authors enabling a statement to be carried within the paginated pages of all published articles.

Please ensure that a 'Declaration of Conflicting Interests' statement is included at the end of your manuscript, after any acknowledgements and prior to the references. If no conflict exists, please state that 'The Author(s) declare(s) that there is no conflict of interest'. For guidance on conflict of interest statements, please see the ICMJE recommendations here

2.6 Research ethics and patient consent

Medical research involving human subjects must be conducted according to the World Medical Association Declaration of Helsinki

Submitted manuscripts should conform to the ICMJE Recommendations for the Conduct, Reporting, Editing, and Publication of Scholarly Work in Medical Journals, and all papers reporting animal and/or human studies must state in the methods section that the relevant Ethics Committee or Institutional Review Board provided (or waived) approval. Please ensure that you have provided the full name and institution of the review committee, in addition to the approval number.

For research articles, authors are also required to state in the methods section whether participants provided informed consent and whether the consent was written or verbal.

Information on informed consent to report individual cases or case series should be included in the manuscript text. A statement is required regarding whether written informed consent for patient information and images to be published was provided by the patient(s) or a legally authorized representative. Please do not submit the patient's actual written informed consent with your article, as this in itself breaches the patient's confidentiality. The Journal requests that you confirm to us, in writing, that you have obtained written informed consent but the written consent itself should be held by the authors/investigators themselves, for example in a patient's hospital record. The confirmatory letter may be uploaded with your submission as a separate file.

Please also refer to the ICMJE Recommendations for the Protection of Research Participants

All research involving animals submitted for publication must be approved by an ethics committee with oversight of the facility in which the studies were conducted. The journal has adopted the Consensus Author Guidelines on Animal Ethics and Welfare for Veterinary Journals published by the International Association of Veterinary Editors.

2.7 Clinical trials

Journal of Geriatric Psychiatry and Neurology conforms to the ICMJE requirement that clinical trials are registered in a WHO-approved public trials registry at or before the time of first patient enrolment as a condition of consideration for publication. The trial registry name and URL, and registration number must be included at the end of the abstract.

2.8 Reporting guidelines

The relevant EQUATOR Network reporting guidelines should be followed depending on the type of study. For example, all randomized controlled trials submitted for publication should include a completed CONSORT flow chart as a

cited figure and the completed CONSORT checklist should be uploaded with your submission as a supplementary file. Systematic reviews and meta-analyses should include the completed PRISMA flow chart as a cited figure and the completed PRISMA checklist should be uploaded with your submission as a supplementary file. The EQUATOR wizard can help you identify the appropriate guideline.

Other resources can be found at NLM's Research Reporting Guidelines and Initiatives

2.9. Research Data

The journal is committed to facilitating openness, transparency and reproducibility of research, and has the following research data sharing policy. For more information, including FAQs please visit the SAGE Research Data policy pages.

Subject to appropriate ethical and legal considerations, authors are encouraged to:

- share your research data in a relevant public data repository
- include a data availability statement linking to your data. If it is not possible to share your data, we encourage you to consider using the statement to explain why it cannot be shared.
- cite this data in your research

Appendix 2.2 – Template for email to NHS GG&C Older People's Psychology Service Clinical Psychologists

TO: [CLINICAL PSYCHOLOGIST]

CC: JON EVANS; STEPHANIE CRAWFORD;

TITLE: MRP PROJECT – [CMHT/AREA]

Hi [CLINICAL PSYCHOLOGIST]

I am a third year Older Adult aligned DClinPsy trainee, and I am writing to request your assistance in identifying potential participants for my MRP.

My project ('Visual Perceptual Assessment in Dementia') aims to assess the sensitivity and specificity of the visuo-spatial sub-test of the ACE-III at detecting visual impairment in people diagnosed with dementia or MCI.

The project will be supervised by Professor Jonathan Evans and Dr Stephanie Crawford, and has received approval from the West of Scotland Research Ethics Committee and the NHS GG&C Caldicott Guardian.

As face to face data collection is no longer feasible for this project, I intend to utilise only existing data from individuals who have undergone neuropsychological assessment (including ACE-III) and who went on to receive a diagnosis of dementia or MCI.

Following discussion with the supervisors and Information Services, it has been agreed that the most appropriate method to identify potential participants would be to individually contact Clinical Psychologists based within each NHS GG&C Older Adult CMHT to request this.

I would be grateful therefore if you could populate the attached Word document with the names and CHI numbers of individuals who satisfy, and do not violate, the following inclusion and exclusion criteria:

Inclusion Criteria:

- Diagnosis of dementia or Mild Cognitive Impairment
- Above diagnosis given following neuropsychological assessment (which includes ACE-III and at least one additional neuropsychological assessment measure)

Exclusion Criteria:

- ACE-III and neuropsychological assessment completed more than 6 months apart
- Diagnosis of a learning disability
- Physical impairment which may significantly impact motor performance (e.g. during writing tasks in visuo-spatial sub-test of ACE-III)

When complete, the attached Word template can be saved as an attachment and returned to this email address (kevin.murray@ggc.scot.nhs.uk).

Any records dating back to 2012 could potentially be included (assuming that the ACE-III has not been used in your service prior to this date), however I would be extremely grateful for as many or as few records as you can provide.

This is based on the assumption that most services maintain a local record (e.g. spreadsheet/word document) of individuals who have been assessed for dementia/MCI, and that the information requested could be quickly provided. However if this is not the case, or if this information is not easily obtainable, please let me know so that I can monitor the feasability of the project.

Thank you for any help you can provide.

Regards,

Kevin Murray
Trainee Clinical Psychologist

Appendix 2.3 – Data Collection template for email to NHS GG&C Older People's Psychology Service Clinical Psychologists

Data Collection Template

Visual Perceptual Assessment in Dementia

Please use this form to record the names and CHI numbers of potential participants for the 'Visual Perceptual Assessment in Dementia' study. This form should be returned to: kevin.murray@ggc.scot.nhs.uk

First Name	Surname	CHI Number

Appendix 2.4 – West of Scotland Ethics Committee Approval Letter

WoSRES
West of Scotland Research Ethics Service

NHS
Greater Glasgow and Clyde

Professor Jonathan Evans
Professor of Applied Neuropsychology
University of Glasgow
Institute of Health and Wellbeing, University of Glasgow
1st Floor, Administration Building,
Gartnaval Royal Hospital
1055 Great Western Road, Glasgow
G12 0XH

West of Scotland REC 1
Research Ethics
Clinical Research and Development
Ward 11
Dykebar Hospital
Grahamston Road
Paisley PA2 7DE

Date 5 November 2020
Direct line 0141 314 0212
E-mail WoSREC1@ggc.scot.nhs.uk

Dear Professor Evans

Study title: **Visual Perceptual Assessment in Dementia**
REC reference: **20/WS/0156**
Protocol number: **N/A**
IRAS project ID: **281385**

The Research Ethics Committee reviewed the above application at the meeting held on 03 November 2020. Thank you to Mr Kevin Murray (student) for attending to discuss the application.

Ethical opinion

The members of the Committee present gave a favourable ethical opinion of the above research on the basis described in the application form, protocol and supporting documentation, subject to the conditions specified below.

Conditions of the favourable opinion

Recommendations:

Number	Recommendation
1	The Committee strongly recommended that a professional statistician assists with the study analysis as there are a few inaccuracies within the statistics mentioned in the application. This is a recommendation and not a condition of approval.
2	The Committee understands that the 4 standard tests are used only to allocate the groups for the study but it thought it would be interesting to investigate if there was difference between the different tests as to what group they would be assigned and this could be looked at as another secondary outcome. This is a recommendation and not a condition of approval.

The REC favourable opinion is subject to the following conditions being met prior to the start of the study.

Confirmation of Capacity and Capability (in England, Northern Ireland and Wales) or NHS management permission (in Scotland) should be sought from all NHS organisations involved in the study in accordance with NHS research governance arrangements. Each NHS organisation must confirm through the signing of agreements and/or other documents that it has given permission for the research to proceed (except where explicitly specified otherwise).

Guidance on applying for HRA and HCRW Approval (England and Wales)/ NHS permission for research is available in the Integrated Research Application System.

For non-NHS sites, site management permission should be obtained in accordance with the procedures of the relevant host organisation.

Sponsors are not required to notify the Committee of management permissions from host organisations.

Registration of Clinical Trials

It is a condition of the REC favourable opinion that **all clinical trials are registered** on a publicly accessible database. For this purpose, 'clinical trials' are defined as the first four project categories in IRAS project filter question 2. Registration is a legal requirement for clinical trials of investigational medicinal products (CTIMPs), except for phase I trials in healthy volunteers (these must still register as a condition of the REC favourable opinion).

Registration should take place as early as possible and within six weeks of recruiting the first research participant at the latest. Failure to register is a breach of these approval conditions, unless a deferral has been agreed by or on behalf of the Research Ethics Committee (see here for more information on requesting a deferral: https://www.hra.nhs.uk/planning-and-improving-research/research-planning/research-registration-research-project-identifiers/

As set out in the UK Policy Framework, research sponsors are responsible for making information about research publicly available before it starts e.g. by registering the research project on a publicly accessible register. Further guidance on registration is available at: https://www.hra.nhs.uk/planning-and-improving-research/research-planning/transparency-responsibilities/

You should notify the REC of the registration details. We routinely audit applications for compliance with these conditions.

Publication of Your Research Summary

We will publish your research summary for the above study on the research summaries section of our website, together with your contact details, no earlier than three months from the date of this favourable opinion letter.

Should you wish to provide a substitute contact point, make a request to defer, or require further information, please visit: https://www.hra.nhs.uk/planning-and-improving-research/application-summaries/research-summaries/

N.B. If your study is related to COVID-19 we will aim to publish your research summary within 3 days rather than three months.

During this public health emergency, it is vital that everyone can promptly identify all relevant research related to COVID-19 that is taking place globally. If you haven't already done so, please register your study on a public registry as soon as possible and provide the HRA with the registration detail, which will be posted alongside other information relating to your project. We are also asking sponsors not to request deferral of publication of research summary for any projects relating to COVID-19. In addition, to facilitate finding and extracting studies related to COVID-19 from public databases, please enter the WHO official acronym for the coronavirus disease (COVID-19) in the full title of your study. Approved COVID-19 studies can be found at: https://www.hra.nhs.uk/covid-19-research/approved-covid-19-research/

It is the responsibility of the sponsor to ensure that all the conditions are complied with before the start of the study or its initiation at a particular site (as applicable).

After ethical review: Reporting requirements

The attached document "After ethical review – guidance for researchers" gives detailed guidance on reporting requirements for studies with a favourable opinion, including:

- Notifying substantial amendments
- Adding new sites and investigators
- Notification of serious breaches of the protocol
- Progress and safety reports
- Notifying the end of the study, including early termination of the study
- Final report

The latest guidance on these topics can be found at https://www.hra.nhs.uk/approvals-amendments/managing-your-approval/.

Ethical review of research sites

NHS/HSC Sites

The favourable opinion applies to all NHS/HSC sites taking part in the study, subject to confirmation of Capacity and Capability (in England, Northern Ireland and Wales) or NHS management permission (in Scotland) being obtained from the NHS/HSC R&D office prior to the start of the study (see "Conditions of the favourable opinion" above).

Non-NHS/HSC sites (if applicable)

I am pleased to confirm that the favourable opinion applies to any non NHS/HSC sites listed in the application, subject to site management permission being obtained prior to the start of the study at the site.

Approved documents

The documents reviewed and approved at the meeting were:

Document	*Version*	*Date*
Confirmation of any other Regulatory Approvals (e.g. CAG) and all correspondence [Caldicott Guardian Approval Letter]		12 August 2020
Evidence of Sponsor insurance or indemnity (non NHS Sponsors only) [Sponsor Insurance/Indemnity]		15 July 2020
IRAS Application Form [IRAS_Form_12102020]		12 October 2020
Letters of invitation to participant [Data Collection Template for email to Clinical Psychologists]	1.2	09 October 2020

Document	*Version*	*Date*
Letters of invitation to participant [Email to Clinical Psychologists]	1.2	09 October 2020
Non-validated questionnaire [Data Collection Template]	1.1	24 September 2020
Research protocol or project proposal [Protocol]	1.2	10 October 2020
Summary CV for Chief Investigator (CI) [Chief Investigator CV]		24 September 2020
Summary CV for student [CV Kevin Murray]	1.1	13 October 2020

Membership of the Committee

The members of the Ethics Committee who were present at the meeting are listed on the attached sheet.

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

User Feedback

The Health Research Authority is continually striving to provide a high quality service to all applicants and sponsors. You are invited to give your view of the service you have received and the application procedure. If you wish to make your views known please use the feedback form available on the HRA website: http://www.hra.nhs.uk/about-the-hra/governance/quality-assurance/

HRA Learning

We are pleased to welcome researchers and research staff to our HRA Learning Events and online learning opportunities – see details at: https://www.hra.nhs.uk/planning-and-improving-research/learning/

IRAS project ID: 281385 **Please quote this number on all correspondence**

With the Committee's best wishes for the success of this project.

Yours sincerely

Veronika Burgess
Coordinator Assistant

On behalf of
Dr Malcolm Booth
Chair

Enclosures: List of names and professions of members who were present at the meeting and those who submitted written comments.
"After ethical review – guidance for researchers"

Copy to: Dr Colette Montgomery Sardar, University of Glasgow
Mr Kevin Murray
nhsg.NRSPCC@nhs.net

West of Scotland REC 1

Attendance at Committee meeting on 03 November 2020

Committee Members:

Name	*Profession*	*Present*	*Notes*
Dr Malcolm Booth	Consultant in Anaesthesia and Intensive Care (Chair)	Yes	Chair of Meeting
Dr Katriona Brooksbank	Clinical Trial Manager (Vice Chair)	Yes	
Miss Clodagh Duffy	Pre-Registration Clinical Scientist	Yes	
Dr Ross Fairgrieve	Consultant in Paediatric Anaesthesia and Pain Management	Yes	
Dr Natasha Fullerton	Consultant Neuroradiologist	Yes	
Mrs Elspeth Fulton	Retired Senior Clinical Research Associate (CRA)	Yes	
Miss Linda Galbraith	Former Management Consultant	Yes	
Mrs Lynda Hamilton	Retired Manager	No	
Dr Peter Hutchison	GP	Yes	
Mrs Katharine Kilgour	Registered Physiotherapist	Yes	
Dr Derek Manson-Smith	Information Research Consultant (Retired)	Yes	
Dr John D McClure	Statistician	Yes	
Mr Steve McGlynn	Specialist Principal Pharmacist (Cardiology)	Yes	
Mrs Laura Rooney	CRUK Lead Research Nurse	Yes	
Dr Patricia Roxburgh	Medical Oncologist	Yes	

Also in attendance:

Name	*Position (or reason for attending)*
Mrs Kirsty Burt	Senior Co-ordinator
Dr Judith Godden	Scientific Officer

Appendix 2.5 – NHS GG&C Board Approval Letter

Senior Research Administrator: Kayleigh McKenna
Telephone Number: 0141 314 4000
E-Mail: Kayleigh.mckenna@ggc.scot.nhs.uk
Website: https://www.nhsggc.org.uk/about-us/professional-support-sites/research-innovation

Research & Innovation
Dykebar Hospital, Ward 11
Grahamston Road
Paisley, PA2 7DE
Scotland, UK

08/12/2020

Mr Kevin Murray
Gartnavel Royal Hospital
1055 Great Western Road
Glasgow
G12 0XH

NHS GG&C Board Approval

Dear Dr Kevin Murray

Study Title:	Visual Perceptual Assessment in Dementia
Principal Investigator:	Mr Kevin Murray
GG&C HB site	Community Mental Health
Sponsor	NHS Greater Glasgow and Clyde
R&I reference:	GN20MH518
REC reference:	20/WS/0156
Protocol no: (including version and date)	V1.2; 10.10.20

I am pleased to confirm that Greater Glasgow & Clyde Health Board is now able to grant **Approval** for the above study.

Conditions of Approval

1. **For Clinical Trials** as defined by the Medicines for Human Use Clinical Trial Regulations, 2004
   a. During the life span of the study GGHB requires the following information relating to this site
      i. Notification of any potential serious breaches.
      ii. Notification of any regulatory inspections.

It is your responsibility to ensure that all staff involved in the study at this site have the appropriate GCP training according to the GGHB GCP policy (www.nhsggc.org.uk/content/default.asp?page=s1411), evidence of such training to be filed in the site file. Researchers must follow NHS GG&C local policies, including incident reporting.

2. **For all studies** the following information is required during their lifespan.
   a. First study participant should be recruited within 30 days of approval date.
   b. Recruitment Numbers on a monthly basis
   c. Any change to local research team staff should be notified to R&I team
   d. Any amendments – Substantial or Non Substantial
   e. Notification of Trial/s study end including final recruitment figures

f. Final Report & Copies of Publications/Abstracts
g. You must work in accordance with the current NHS GG&C COVID19 guidelines and principles.

Please add this approval to your study file as this letter may be subject to audit and monitoring.

Your personal information will be held on a secure national web-based NHS database.

I wish you every success with this research study

Yours sincerely,

Kayleigh McKenna
Senior Research Administrator

Appendix 2.6 – NHS GG&C Caldicott Guardian Approval Letter

NHS
Greater Glasgow and Clyde

Kevin Murray
kevin.murray@ggc.scot.nhs.uk

Data Protection Officer
Information Governance Department
NHS Greater Glasgow & Clyde
2nd Floor, 1 Smithhills Street
Paisley PA1 1EB

Date: 12/08/2020

Enquiries to: Isobel Brown
Tel: 0141 355 2020
Email: Isobel.Brown@ggc.scot.nhs.uk

Dear Kevin

Re: Visual Perceptual Assessment in Dementia

Thank you for your Caldicott application received on 28/07/2020 regarding your proposed Audit.

I have reviewed this application and can confirm that I am happy to approve this application on behalf of the Caldicott Guardian.

Approval is base on the following conditions;

- That the CHI numbers and full postcode are not shared externally

Please note that this approval only covers access to NHSGGC patients.

Please find attached a signed copy of your application for your records.

Yours sincerely

Isobel Brown
Data Protection Officer
Information Governance

Appendix 2.7 – Study Protocol

RESEARCH STUDY PROTOCOL

TITLE

Visual Perceptual Assessment in Dementia

INTRODUCTION

Rationale

Although several well-validated tests are available for measuring common symptoms of dementia and Mild Cognitive Impairment (MCI) such as memory, language, executive function and attention, the methods available for assessing visuo-perceptual ability are relatively limited. The Addenbrooke's Cognitive Examination (Third edition: ACE-III; Hsieh at al., 2013) is a widely used cognitive screening tool, and although this includes a measure of visuo-spatial ability it is unclear how accurately this detects visual perceptual deficits in individuals with dementia and MCI.

Background information including literature review

Almost one third of the neocortex is involved in visual processes (Van Essen and Drury, 1997). It is perhaps unsurprising therefore that as many as 32.5% of individuals diagnosed with dementia experience visuo-perceptual decline as part of their disease aetiology (Bowen et al, 2016), with incidence rates highest in those diagnosed with Alzheimer's Dementia (Alzheimer's Society, 2018). Impairment in visual processing is associated with an increased risk of falls for those diagnosed with dementia (Fernando et al, 2017) and can reduce mobility (van Ooteghem et al, 2019). Accurate measurement of visuo-perceptual ability is therefore essential to informing clinical decisions, and may also assist with differential diagnosis and risk management.

Potential risk and benefits

This study aims to assess the accuracy of the ACE-III at detecting visuo-perceptual deficits in individuals with dementia and MCI, thereby improving understanding of the methods available for informing clinical judgement. In doing so it is hoped that the overall accuracy of dementia diagnosis, including differential diagnosis, will be enhanced. As there will be no direct contact with participants, and existing data will be used for analysis, there are no risks to participants anticipated.

AIM/PRIMARY AND SECONDARY OBJECTIVES

This study aims to assess how well the ACE-III detects visuo-perceptual deficits in individuals with dementia or MCI. This will be achieved by comparing the performance of individuals with and without visuo-perceptual impairment on the visuospatial sub-test of the ACE-III. The current study therefore will test the hypothesis that individuals with visual impairment will obtain significantly lower scores on the visuo-perceptual sub-test of the ACE-III than individuals with no visual impairment.

METHODOLOGY

Inclusion and Exclusion Criteria

Participants will include clients who have been under the care of NHS Greater Glasgow and Clyde Older Adult Community Mental Health Teams (CMHTs). In order to be included in the study participants are required to have completed the ACE-III and a separate visuo-spatial sub-test as part of their neuropsychological assessment, and have a diagnosis of dementia or mild cognitive impairment (MCI).

Those who meet the following criteria will be excluded from participation in the study:

- Individuals for whom visual-perceptual impairment is unknown or unclear
- ACE-III and neuropsychological assessment completed more than 6 months apart
- Diagnosis of a learning disability
- Physical impairment which may impact motor performance e.g. during writing tasks in visuo-spatial sub-test of ACE-III

Study design / Plan – Study Visits

A between-groups observational design will be utilised in order to determine how accurately the ACE-III can identify visual perceptual impairment. The study will utilise existing data from neuropsychological assessments, and there will be no requirement for face to face contact with participants or direct assessment.

Research will be conducted by a trainee clinical psychologist, who will be supervised throughout the project by a qualified clinical psychologist to ensure safe and appropriate research principles are followed. The British Psychological Society's *'Code of Human Research Ethics'* (BPS, 2014) and '*Code of Ethics and Conduct'* (BPS, 2018) will also guide the researcher's practice, and local ethical and Caldicott Guardian approval will be sought to ensure appropriate research standards are maintained.

Once potential participants have been identified, the relevant data will be recorded on a password protected Microsoft Excel database on an NHS computer. An anonymised data set will be created for analysis using study ID numbers and transferred to a university network file via email from a secure NHS email account, and postcodes will be removed and replaced with relevant SIMD ranking. CHI numbers will also be removed, and no personally identifiable data will be transferred out-with an NHS computer.

The visuo-spatial sub-test of the ACE-III represents the dependent variable of the study. In this sub-test, individuals complete five tasks which rely on visuo-spatial abilities. These include drawing an analogue clock, copying two diagrams (infinity diagram and wire cube), dot counting and fragmented letter identification. Scores on this measure, which can range from 0 – 16, will be used to assess the sensitivity and specificity of the ACE-III at detecting visual impairment in dementia.

The independent variable, i.e. allocation to the impaired or unimpaired group, will be determined by performance on visual perceptual sub-tests included in participant's full neuropsychological assessment batteries. Participants will be considered impaired if their visual perceptual performance falls in the bottom 5th percentile (or, Z-Score <-1.67; T-Score<33; Scaled Score<5: Standard Score<75). The most commonly used neuropsychological assessments which involve tests of visual perceptual impairment include the Repeatable Battery for the Assessment of Neuropsychological Status (RBANS), Wechsler Adult Intelligence Scale Fourth Edition (WAIS-IV), Severe Impairment Battery (SIB) and Kaplan Baycrest Neurocognitive Assessment (KBNA).

Demographic factors including age and gender will be recorded. Postcode will also be recorded in order to determine Scottish Index of Multiple Deprivation (SIMD) rank. Disease-specific factors (i.e. diagnosis) will also be recorded.

Durations of participation

There will be no face to face contact with participants, and only existing data from participant's health records will be used for the study. Therefore, participants are not required to spend any time on the project.

Study Drugs

Not applicable

Concomitant Medications

Not applicable

Criteria for discontinuation

Not applicable

Procedure for collecting data and storage

A trainee clinical psychologist ('researcher') will be responsible for collecting and analysing the data. Following approval from the local ethics committee and Caldicott Guardian, clinical psychologists based within OACMHTs across the eight NHS GG&C Health and Social Care Partnerships (East Dunbartonshire, East Renfrewshire, Inverclyde, Glasgow North East, Glasgow North West, Glasgow South, Renfrewshire, West Dunbartonshire) will be contacted individually by the trainee to request details of clients within their service who satisfy the inclusion criteria, and who do not violate the exclusion criteria.

The health records of these individuals will then be accessed by the researcher, and following an additional check for inclusion and exclusion criteria the details of those appropriate for the study will be added to a password protected Microsoft Excel database on an NHS laptop computer. The list of potential participants in the database will then be randomised using the 'Randomise' function within Microsoft Excel, and the first 150 individuals on this list will be included in the study.

STATISTICAL CONSIDERATIONS

Sample Size

Bujang and Adnan (2016) note that sensitivity is the most appropriate measure of diagnostic utility for screening tests (over and above specificity). They provide indicators of minimum sample sizes for sensitivity analysis based on prevalence of the condition of interest in the population being sampled, and for different levels of sensitivity. Based on an estimated prevalence of visual impairment in people with dementia of 30% (Brown et al., 2016), 45 people with visual impairment, and a total sample of 150, is proposed as a minimum sample size for determining the sensitivity if sensitivity is at least 0.8 (power of 0.826, p=0.0034).

A sample of 45 people with impairment and 105 without would have 90% power to detect a difference of d=0.76 in an independent samples t-test. In order for the ACE-III to effectively detect differences between the impaired and unimpaired groups, and for clinicians to be confident in the clinical accuracy of these results, a large (d=0.8) effect size for this separation would be required ($p<0.05$, two-tailed).

Between April 2019 and March 2020, 2,187 individuals were diagnosed with dementia or MCI across NHS GG&C. Following discussions with members of a local OACMHT, it is estimated that around 3% of these individuals are likely to have underwent neuropsychological assessment. Therefore, approximately 66 individuals would be expected to receive a neuropsychological assessment per year, and around 528 in the 8 years the ACE-III has been used within NHS GG&C. As such, it is expected that obtaining the required sample size is realistic within the timeline proposed.

Method of Analysis

The statistics package SPSS will be used to analyse the results of the study, and data will initially be checked for normality, skew and kurtosis. If the data are normally distributed, or is non-normally distributed but can be transformed to satisfy the requirements for parametric testing, an independent samples t-test will be used to compare the mean ACE-III scores between the impaired and unimpaired groups.

If the data is not normally distributed and transformation for parametric testing is not possible, then a Mann-Whitney test will be used to compare the medians of each group. The sensitivity and specificity of the ACE-III visuo-perceptual sub-test will be investigated using Receiver Operating Characteristic (ROC) curve analysis. Descriptive statistics will include appropriate parametric or non-parametric measures of dispersion and central tendency.

ETHICS

The study will utilise existing data only and there is no requirement for face to face contact with the researcher. However, approval from the NHS ethics committee will be sought, as well as approval to access and use patient information from the NHS GG&C Caldicott Guardian and from the Research and Innovation service.

Collection, storage and dissemination of data will adhere to the appropriate guidelines stipulated by the Data Protection Act 2018 (UK Government, 2018), in particular schedule 19 within Chapter 2 (‘*Processing for archiving, research and statistical*

purposes: safeguards'). The Research Governance Framework for Health and Community Care (NHS GG&C, 2006) will also be followed to ensure the study upholds the ethical standards required.

FINANCE AND INDEMNITY

The University of Glasgow Doctorate in Clinical Psychology programme student research budget will cover any research costs incurred.

Indemnity will also be provided under the University of Glasgow's *'Legal Liability and No Fault Compensation for Human Clinical Trials'* insurance policy.

PUBLICATIONS

It is intended that the completed study will be published in a peer reviewed scientific journal, as well as on the University of Glasgow's Enlighten database. (https://www.gla.ac.uk/research/enlighten/).

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Appendix 2.8 - Original Research Proposal

Name of Assessment	MRP Proposal
Title of Project	Visual Perceptual Assessment in Dementia
Matriculation Number	2428483
Date of Submission	05/03/2020
Version Number	2
Actual Word Count	3167
Maximum Word Count	3000

ABSTRACT

Background

Up to 32.5% of individuals diagnosed with dementia experience visuo-perceptual decline. Accurate assessment in this area is essential therefore. The Addenbrookes Cognitive Examination (ACE-III) is one of the most widely used screening tools in dementia assessment, and contains a measure of visuo-spatial ability. Little is known about the test's diagnostic accuracy in this area however.

Aims

The current study aims to assess how well the ACE-III can detect visuo-perceptual impairment in individuals with neurocognitive decline.

Methods

Individuals with dementia or mild cognitive impairment (MCI) will complete a Visual Assessment Battery (VAB) and will be allocated to either a visually impaired or visually unimpaired group, based on these results. They will also complete the visuo-spatial sub-test of the ACE-III. Scores on the visuo-spatial sub-test of the ACE-III will then be analysed to compare the impaired and unimpaired groups and to determine the test's sensitivity and specificity to visuospatial impairment.

Applications

The results of the study will help towards understanding of the diagnostic validity of the ACE-III, and if necessary alternative methods for assessment of visuo-spatial ability in individuals with dementia or MCI will be proposed.

1. INTRODUCTION

Almost one third of the neocortex is involved in visual processes (Van Essen and Drury, 1997). It is perhaps unsurprising therefore that as many as 32.5% of individuals diagnosed with dementia experience visuo-perceptual decline as part of their disease aetiology (Bowen et al, 2016), with incidence rates highest in those diagnosed with Alzheimer's Dementia (Alzheimer's Society, 2018). Impairment in visual processing is associated with an increased risk of falls for those diagnosed with dementia (Fernando et al, 2017) and can reduce mobility (van Ooteghem et al, 2019). Accurate measurement of visuo-perceptual ability is therefore essential to informing clinical decisions, and may also assist with differential diagnosis and risk management.

Although several well-validated tests are available for measuring common symptoms of dementia such as memory, language, executive function and attention, the methods available for assessing visuo-perceptual ability are relatively limited. The Addenbrooke's Cognitive Examination (Third edition: ACE-III; Hsieh at al., 2013) is a widely used cognitive screening tool, and although this includes a measure of visuo-spatial ability it is unclear how accurately this detects visuo-perceptual deficits in individuals with dementia.

2. AIMS AND HYPOTHESIS

2.1 Aims

This study aims to assess how well the ACE-III detects visuo-perceptual deficits in individuals with dementia or Mild Cognitive Impairment. This will be achieved by comparing the performance of individuals with and without visuo-perceptual impairment on the visuospatial sub-test of the ACE-III.

2.2 Hypothesis

The ACE-III aims to detect visuo-perceptual impairment in individuals with dementia. Therefore, the current study will test the hypothesis that individuals with visual impairment will obtain significantly lower scores on the visuo-perceptual sub-test of the ACE-III than individuals with no visual impairment.

3. PLAN OF INVESTIGATION

3.1 Participants

Participants will include clients who have been under the care of NHS Greater Glasgow and Clyde Older Adult Community Mental Health Teams (CMHTs).

3.2 Inclusion Criteria

In order to be included in the study participants are required to have a diagnosis of dementia or mild cognitive impairment (MCI). This will be confirmed using the '*diagnosis'* tab within the online 'Clinical Portal' recording system.

3.3 Exclusion Criteria

Those who meet the following criteria will be excluded from participation in the study:

- Deemed to lack capacity to give informed consent
- Diagnosis of a learning disability
- Registered as blind or having a severe visual impairment
- Deaf or severe hearing impairment
- Non-fluent English speakers
- Any other factors that would prevent the individual from fully completing the assessment process

3.4 Recruitment Procedures

Individuals who satisfy the inclusion criteria, and are not disqualified by the exclusion criteria, will be offered an information Sheet and Cover Letter outlining the nature of the study by a member of their local CMHT. The contact details of those who express an interest in taking part will then be forwarded to the researcher, who will get in touch with the individual via their preferred contact method to clarify any additional questions and organise a testing appointment. This will take place either at the patient's home or in their local CMHT clinic.

Once written consent has been obtained the visuo-spatial sub-test of the ACE-III will be administered, followed by De Vries at al's (2017) Visual Assessment Battery (VAB). If the participant has completed the ACE-III within the last three months however this will not need to be repeated. Rather, their visuo-spatial scores will be checked and re-calculated using their existing ACE-III record form.

3.5 Measures

The visuo-spatial sub-test of the ACE-III represents the dependent variable of the study. In this sub-test, individuals complete five tasks which rely on visuo-spatial abilities. These include drawing an analogue clock, copying two diagrams (infinity diagram and wire cube), dot counting and fragmented letter identification. Scores on this measure, which can range from 0 – 16, will be used to assess the sensitivity and specificity of the ACE-III at detecting visual impairment in dementia.

The independent variable, i.e. allocation to the impaired or unimpaired group, will be determined by de Vries et al's (2017) Visual Assessment Battery (VAB) which includes the following tests:

Table 1 – De Vries et al (2017); Visual Assessment Battery (VAB)

Item	Sub-test	Source of test	Disorder assessed	Cut-off score (to determine disorder)
1	Bells Cancellation Test	Kaplan Baycrest Neurocognitive Assessment	Lateralised Attentional Disorders	6 omissions per side
2	Dot Counting Task	Visual Object and Space Perception (VOSP) battery	Non-lateralised Attentional Disorders	9/10
3	Cookie Theft Picture	Boston Diagnostic Aphasia Examination 3 (BDAE-3)	Simultanagnosia	7/11
4	Trail Making Test	Delis Kaplin Executive Function System (DKEFS) battery	Temporal Processing Disorders	6 (Scaled Score)
5	Figure Ground Segmentation	Leuven perceptual organization screening test (L-post).	Perceptual Organisation Disorders	4/5
6	Silhouettes	Visual Object and Space Perception Battery (VOSP)	Object Agnosia	18/30
7	Crowding Task	Cortical Vision Screening Test (CORVIST)	Reduced Visual Loading	1/2 (upper set)
8	Spatial Span	Wechsler Memory Scale Third Edition (WMS-III)	Spatial Memory Disorders	6 (Scaled Score)
9	Taylor Complex Figure	The Repeatable Battery for the Assessment of Neuropsychological Status (RBANS)	Visual Constructive Disorders	6 (Scaled Score)
10	Global Motion Detection	L-Post battery	Movement Perception Disorders	3/5
11	Shape Ratio Discrimination	L-Post battery	Visual Form Agnosia	4/5

Demographic factors, including age, gender and socio-economic status of participants, will be recorded. Disease-specific factors will also be analysed and will include dementia type, age of onset and illness duration.

3.5.1 Bells Cancellation Test – Lateralised Attentional Disorders

The Bells Cancellation Test (Gauthier et al, 1989) is a test of visual attention and is used to detect lateralised attentional disorders (e.g. unilateral neglect). Two-week test-retest reliability was reported as r=0.69 (Gauthier et al, 1989), and Ferber and Karnath (2001) found that the test successfully detected visual neglect in 94% of cases. Individuals are presented with a landscape oriented A4 sheet of paper which contains pictures of 35 'target' objects (i.e. bells) and 264 'distracters' (e.g. bird, key, apple, mushroom). The target objects, i.e. bells, are distributed evenly across the page. Following a practice trial the individual is asked to circle all the bells on the page using a pencil. If six or more bells are omitted from the left or right half of the sheet, then the individual is considered to display visual neglect.

3.5.2 Dot Counting Task (VOSP) – Non-Lateralised Attentional Disorders

The Dot Counting Task within the Visual Object and Space Perception Battery (VOSP; Warrington and James, 1991) includes ten white cards with randomly arranged black dots. Participants are asked to identify how many dots are displayed on each card. Any score below the maximum is considered to indicate impairment in object and space perception. The Dot Counting Task was found to have low internal consistency (<0.59; Bonello et al, 1997), however more research is required to determine its validity and test-retest reliability (Strauss et al, 2006). Specificity was measured as 92.8 based on the cut off scores provided within the manual (Bonello et al, 1997).

3.5.3 Complex Picture Description Task (BDAE-3) – Simultanagnosia

The Complex ('Cookie Theft') Picture Description task is included as a measure of aphasia within the Boston Diagnostic Aphasia Examination (Third edition, BDAE-3; Goodglass et al, 2000). De Vries et al (2017) recommended its inclusion in their Visual Assessment Battery as a means of assessing participant's abilities to perceive more than one object at a time (i.e., to detect the presence of simultanagnosia).

Individuals are asked to describe a scene involving a black and white illustration of a boy is falling from a stool as he reaches for cookies, while a woman is washing dishes next to an overflowing sink. Individuals with simultanagnosia are likely to adopt a piecemeal approach to describing the image and will typically report objects in isolation (e.g. “boy”, “cookie”, “stool”, “dishes”) rather than describing the overall scene.. Scores up to a maximum of 11 are given depending on length of description, accuracy, and content, with 7 or below said to indicate potential simultanagnosia.

3.5.4 Trail Making Test (D-KEFS) – Temporal Processing Disorders

The Trail Making Test is from the Delis-Kaplan Executive Function System (D-KEFS). Participants complete five short tasks which rely on visual scanning strategies to identify and connect numbers and letters. Raw scores for each of the five conditions are determined by the total time to complete each task. Raw scores are then converted to scaled scores, with scaled scores of 6 or below suggestive of a impairment.

3.5.5 Figure Ground Segmentation (L-Post) – Perceptual Organisation Disorders

In the Figure Ground Segmentation sub-test of the Leuven Perceptual Organization Screening Test (L-Post), participants are shown a target image and three additional images, and are asked to identify which of the three additional images are most similar to the target image. This is repeated over five trials, and scores of 4 or less out of 5 are considered to reflect a perceptual organisation disorder.

3.5.6 Silhouettes (VOSP) – Object Agnosia

The *Silhouettes* sub-test of the Visual Object and Space Recognition Battery (VOSP) requires participants to identify 30 silhouetted drawings (15 animals, then 15 common objects) which have been rotated laterally to various angles such that these are viewed

from unusual angles. The test is discontinued after 5 failures in either set, and individuals with right hemisphere lesions identify on average 18/30 silhouettes, compared with 23/30 for controls.

3.5.7 Crowding Task (CORVIST) – Reduced Visual Loading (in time and space)

The Crowding Task within the CORVIST aims to detect impairments in visual acuity/loading, wherein individuals struggle to identify individual visual stimuli when they are accompanied by other objects. Participants are shown an A4 page, at a distance of four metere, displaying four sets of seven numbers and letters (similar to U.K. car registration plates). The spacing of the numbers and letters in the upper two sets are visible for those with 20/40 visual acuity. The lower two sets are spaced further apart, such that 'crowding' effects do not impact on performance. Individuals who are unable identify all numbers and letters in the upper two sets, therefore, are considered to exhibit impairment in visual loading.

3.5.8 Spatial Span (WMS-III) – Spatial (Working) Memory Disorders

The Spatial Span sub-test of the WMS-III is an adaptation of the Corsi Block-tapping test (Milner, 1971). Ten blocks are arranged on a board, which examiners tap in pre-determined orders. Examinees are asked to repeat examiner's sequences over several trails, initially in the same order then in reverse order. The test is considered to be a visually based version of the digit span task, and is used to detect disorders in spatial working memory.

3.5.9 Taylor Complex Figure (RBANS) – Visual Constructive Disorders

The Taylor Complex Figure Test is included within the RBANS. Individuals are shown a complex figure and asked to copy this. Scores out of 20 are offered based on the accuracy and detail of the representation, which is then converted into a scaled score. Low scores on this task is indicative of visual constructive difficulty.

3.5.10 Global Motion Detection (L-Post) – Disorders in Movement Perception

The Global Motion Detection sub-test of the L-Post is used to detect disorders in movement perception. As with the Figure Ground Segmentation sub-test, participants are asked to identify which of three images most closely resemble a target image. This is repeated five times. The images in the Global Motion Detection test include elements which move vertically and horizontally across the image. Scores of 3 or less out of 5 indicate a movement perception disorder.

3.5.11 Shape Ratio Discrimination (L-Post) – Visual Form Agnosia

The Shape Ratio Discrimination sub-test of the L-Post is similar to the other L-Post sub-tests wherein five trials are completed during which the participant is asked to identify which of three shapes most closely resemble a target image. The images in this sub-test include vertical lines of varying lengths and thickness, and scores of 4 or less out of 5 indicate visual form agnosia.

3.6 Design

A between-groups observational design will be utilised in order to determine whether identification of visual impairment by the ACE-III aligns with that identified by the VAB.

If visual impairment is not identified by any of the VAB tests then participants will be placed in the unimpaired group, whereas failure on one or more of the VAB tests will result in allocation to the impaired group. The results obtained by each group will then be used to determine the sensitivity and specificity of the ACE-III visuo-perceptual sub-test.

3.7 Research Procedures

The time taken to collect data from each participant is not expected to exceed one hour. This estimate includes time for breaks between sub-tests in the event of participant fatigue.

Research will be conducted by a Trainee Clinical Psychologist, who will be supervised throughout the project by a qualified Clinical Psychologist to ensure safe and appropriate research principles are followed. The British Psychological Society's *'Code of Human Research Ethics'* (BPS, 2014) and '*Code of Ethics and Conduct'* (BPS, 2018) will also guide the researcher's practice, and local R&D and Research Ethics Committee approval will be sought to ensure appropriate research standards are maintained.

3.8 Data Analysis

The statistics package SPSS will be used to analyse the results of the study, and data will initially be checked for normality, skew and kurtosis. If the data are normally distributed, or is non-normally distributed but can be transformed to satisfy the requirements for parametric testing, an independent samples t-test will be used to compare the mean ACE-III scores between the impaired and unimpaired groups.

If the data is not normally distributed and transformation for parametric testing is not possible, then a Mann-Whitney test will be used to compare the medians of each group. The sensitivity and specificity of the ACE-III visuo-perceptual sub-test will be investigated using Receiver Operating Characteristic (ROC) curve analysis. Descriptive statistics will include appropriate parametric or non-parametric measures of dispersion and central tendency.

3.9 Justification of Sample Size

Bujang and Adnan (2016) note that sensitivity is the most appropriate measure of diagnostic utility for screening tests (over and above specificity). They provide indicators of minimum sample sizes for sensitivity analysis based on prevalence of the condition of interest in the population being sampled, and for different levels of sensitivity. Based on an estimated prevalence of visual impairment in people with dementia of 30% (Brown et al., 2016), 20 people with visual impairment, and a total sample of 67, is proposed as a minimum sample size for determining the sensitivity if sensitivity is at least 0.8 (power of 0.804, p=0.041).

A sample of 20 people with impairment and 47 without would have 90% power to detect a difference of d=0.76 in an independent samples t-test. In order for the ACE-III to effectively detect differences between the impaired and unimpaired groups, and for clinicians to be confident in the clinical accuracy of these results, a large (d=0.8) effect size for this separation would be required ($p<0.05$, two-tailed).

As participants will be recruited from the various Older Adult Community Mental Health Teams (OACMHTs) across NHS GG&C, and considering that neurocognitive decline is one of the most common reasons for referral to these teams, it is expected that the required sample size will be obtained within the timeline proposed.

3.10 Settings and Equipment

Data collection will take place either in clinical rooms within Older Adult CMHT clinics or at participant's homes. For administration of the assessment measures a black biro pen, and paper copies of the ACE-III and each of the VAB tests, will be required. Original copies of these, as well as the Information Sheet and signed Consent Forms, will be stored in a locked filing cabinet by the researcher. Copies of each will also be made available for storage in the participant's clinical health file.

For participants who have completed the ACE-III within three months of participation in the study, the researcher will review and score the original ACE-III record form from their clinical health file (or from a scanned copy in their electronic 'EMIS' health record). A copy will also be printed and stored in a locked filing cabinet alongside the research data. A password protected laptop and an encrypted password protected USB memory stick will be used to store data electronically.

4. HEALTH AND SAFETY ISSUES

4.1 Researcher Safety Issues

The researcher will adhere to NHS guidelines regarding lone working, health and safety and fire safety. For visits to participant's homes, the researcher will ensure they have completed NHS GG&C's '*Violence Reduction*' training.

4.2 Participant Safety Issues

The researcher will remain mindful of the potential distress associated with neuropsychological assessment, and will provide regular reassurance and cease testing if the participant becomes distressed.

5. ETHICAL ISSUES

Collection, storage and dissemination of data will adhere to the appropriate guidelines stipulated by the Data Protection Act 2018 (UK Government, 2018), in particular schedule 19 within Chapter 2 ('*Processing for archiving, research and statistical purposes: safeguards'*). The Research Governance Framework for Health and Community Care (NHS GG&C, 2006) will also be followed to ensure the study upholds the ethical standards required.

Although participants will have a confirmed diagnosis of dementia or MCI, the exclusion criteria will ensure that all those included in the study will retain capacity to give informed consent to participate in the study. Given the memory impairments inherent within this

population group however regular reminders of their right to withdraw will be provided throughout the assessment process. Other functional and cognitive impairments, including disorientation, attention, praxis and side effects of medication, will also be considered to ensure that any stressors are avoided.

Participants who do not have visuo-perceptual deficits recorded in their clinical notes, but who display visual impairment in the assessment measures, will be asked if they wish for this information to be communicated to the clinical team within the relevant CMHT. This will enable the clinical team to offer appropriate advice and support, or to refer the individual for further visual assessment.

6. FINANCIAL ISSUES

The University of Glasgow student research budget will cover the cost of printing Information Sheets, Cover Letters, Consent forms and the assessment measures. No other significant costs are anticipated.

7. TIMETABLE

The project is due to be completed by July 2021. A Viva voce exam will then take place in September 2021, with any final corrections to be made by the following month. The proposed timeline of the project is outlined in Table 2:

Table 2 – Proposed project timeline

2019	
April	Outline (1500 words)
May	
June	
July	
August	
September	
October (*2nd Year*)	
November	
December	Proposal (for blind review: 3000 words)
2020	
January	
February	Proposal feedback
March	Proposal amendments
April	Letter from Research Director
May	Submit for sponsor approval
June	Submit for ethics/R&D application
July	Data Collection
August	Data Collection
September	Data Collection
October (*3rd Year*)	Data Collection
November	Data Collection
December	Data Collection
2021	
January	Data Collection
February	Data Collection
March	Data Collection
April	Analysis
May	Write up
June	Write up
July	Submission
August	Draft for publication
September	Viva voce
October	Corrections
November	Graduation

8. PRACTICAL APPLICATIONS

This study will assess the accuracy of the ACE-III at detecting visuospatial deficits in individuals with dementia and MCI, thereby improving understanding of the methods available for informing clinical judgement. In doing so it is hoped that the overall accuracy of dementia diagnosis, including differential diagnosis, will be enhanced.

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10. APPENDICES

APPENDIX 1 – HEALTH AND SAFETY FORM

WEST OF SCOTLAND/ UNIVERSITY OF GLASGOW

DOCTORATE IN CLINICAL PSYCHOLOGY

HEALTH AND SAFETY FOR RESEARCHERS

1. Title of Project	Visual Perceptual Assessment in Dementia
2. Trainee	Kevin Murray
3. University Supervisor	Professor Jon Evans
4. Other Supervisor(s)	Dr Stephanie Crawford, Dr Claire McGuire
5. Local Lead Clinician	Dr Stephanie Crawford
6. Participants: (age, group or sub-group, pre- or post-treatment, etc)	Adults with diagnosis of Dementia or Mild Cognitive Impairment.
7. Procedures to be applied (eg, questionnaire, interview, etc)	Cognitive Assessment Tests: Bell's Cancellation Test (Kaplan Baycrest Neurocognitive Assessment), Dot Counting Task (Visual Object and Space Perception (VOSP) battery), Cookie Theft Picture (Boston Diagnostic Aphasia Examination 3 (BDAE-3)), Trail Making Test (Delis Kaplin Executive Function System (DKEFS) battery), Figure Ground Segmentation (Leuven perceptual organization screening test (L-post)), Silhouettes (Visual Object and Space Perception Battery (VOSP)), Crowding Task (Cortical Vision Screening Test (CORVIST)), Spatial Span (Wechsler Memory Scale Third Edition (WMS-III)), Taylor Complex Figure

	(The Repeatable Battery for the Assessment of Neuropsychological Status (RBANS)), Global Motion Detection (L-Post battery), Shape Ratio Discrimination (L-Post battery)
8. Setting (where will procedures be carried out?) i) General	Clinical interview rooms within NHS Greater Glasgow and Clyde CMHT clinical bases Care homes/clients homes/day centres (where participant's access to above settings is not possible)
ii) Are home visits involved	Yes (dependant on participant's ability to attend settings, as detailed above)
9. Potential Risk Factors Considered (for researcher and participant safety): i) Participants ii) Procedures iii) Settings	i) It is expected that the majority of participants will be elderly and will experience cognitive and physical impairments. Associated risks (including relating to mobility, risk of falls, vulnerability) will therefore be considered and where attendance at clinical settings may pose a risk to participants home/day centre visits will be offered. ii) Potential distress resulting from the assessment process will also be considered, and if distress is noted participants will be reassured and reminded that they may withdraw at any time. iii) Where possible, data collection will take place within a clinical setting. Where home visits are required however the researcher will ensure that they have completed the appropriate NHS GG&C 'Violence Reduction' and 'Reducing Risks of Violence and Aggression' training and that they adhere to the NHS GG&C Lone Working policy.

Trainee signature: Kevin Murray..... Date:19/12/19.....

University supervisor signature: ..... Date:19/12/19.....

APPENDIX 2 – RESEARCH EQUIPMENT, CONSUMABLES AND EXPENSES FORM

RESEARCH EQUIPMENT, CONSUMABLES AND EXPENSES

Trainee

Kevin Murray……..……

Year of Course ……2nd …… **Intake Year**……2018……...……..

Please refer to latest stationary costs list (available from student support team)

Item	Details and Amount Required	Cost or Specify if to Request to Borrow from Department
Stationary	£0	Subtotal: £0
Postage	£0	Subtotal: £0
Photocopying and Laser Printing	Participant information sheet (1 single sided page x 67; 67 x 1 x £0.05 = **£3.35**) Consent forms (1 single sided sheet x 67; 67 x 1 x £0.05 = **£3.35**) ACE-III (3 double sided sheets x 67; 67 x 3 x £0.07 = **£14.07**) Bell's Cancellation Test (2 double sided sheets x 67; 67 x 2 x £0.07 = **£9.38**)	Subtotal: £30.15
Equipment and Software	£0	Subtotal: £0
Measures	Bell's Cancellation Test (Kaplan Baycrest Neurocognitive Assessment)* Figure Ground Segmentation; Global Motion Detection; Shape Ratio Discrimination (Leuven perceptual	* Free to access and use online ** To be borrowed from Department of Clinical Psychology, University of Glasgow *** To be borrowed from West Dunbartonshire

	organization screening test (L-post))* Dot Counting Task; Silhouettes (Visual Object and Space Perception (VOSP) battery)** Trail Making Test (Delis Kaplin Executive Function System (DKEFS) battery)** Crowding Task (Cortical Vision Screening Test (CORVIST))** Spatial Span (Wechsler Memory Scale Third Edition (WMS-III))** Taylor Complex Figure (The Repeatable Battery for the Assessment of Neuropsychological Status (RBANS))** Cookie Theft Picture (Boston Diagnostic Aphasia Examination 3 (BDAE-3))***	Older Adults CMHT, NHS GG&C
Miscellaneous	£0	Subtotal: £0
Total	**£30.15**	**£30.15**

For any request over £200 please provide further justification for all items that contribute to a high total cost estimate. Please also provide justification if costing for an honorarium:

Trainee Signature……Kevin Murray……..…. Date…05/03/2020……

Supervisor's Signature ……..……..... Date …….....……